ABSTRACTS OF WORLD MEDICINE

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2348. **The Rate of Bactericidal Action of Triethylene Glycol Vapor on Microorganisms Dispersed into the Air in Small Droplets**

W. LESTER, O. H. ROBERTSON, T. T. PUCK, and H. WISE. *American Journal of Hygiene* [*Amer. J. Hyg.*] **50**, 175–188, Sept., 1949. 7 figs., 14 refs.

Freshly atomized triethylene glycol has a rapid bactericidal action which is difficult to measure accurately as the chemical rapidly condenses on surfaces in the experimental chamber, thus reducing the concentration in the atmosphere. By means of a special apparatus whereby the concentration of triethylene glycol and water vapour could be maintained constant in the atmosphere, the bactericidal action of glycol vapour at various degrees of saturation and under varying conditions of humidity was measured. With a relative humidity of between 5% and 50% the bactericidal action rose progressively with the concentration of glycol vapour, but as the relative humidity was raised above 50% there was a rapid diminution of bactericidal action at all concentrations of glycol vapour.

Scott Thomson

2349. **Triethyelene Glycol in Air Disinfection.** (Försök med trietylenglykolluftdesinfektion)

E. GEDDA. *Nordisk Medicin* [*Nord. Med.*] **41**, 363–368, Feb. 25, 1949. 5 figs., 12 refs.

Two series of tests were carried out to determine the efficacy of vaporized triethylene glycol for the disinfection of air in public places. One of the places was a waiting room for out-patients at the Ear, Nose and Throat Clinic, Sahlgren Hospital, Gothenburg, with a volume of about 400 cubic metres and of very irregular shape, and the other a nursery at Vidkärr Children's Home, Gothenburg.

In the former series similar control tests were made in the same waiting room for the same number of days, but without the use of glycol; in the latter series a control room identical in every respect with the test nursery was used.

In the waiting-room tests the bacterial concentration in the air was reduced by about 30% by use of triethylene glycol, and at the children's home a reduction of about 40% in the test nursery compared with the control room was obtained. The difference in each case is statistically significant.

The atomizer employed was a modified " aromator " electrically heated and fitted with an electric fan. It provided sufficient but inconstant concentrations in the peripheral parts of the waiting room. For the bacterial count a Bourdillon apparatus was employed, colonies in blood-agar cultures being counted (without differential counts of the various species), after 24 hours in an incubator at 37° C. The relative humidity ranged from 35 to 60% in the first series and 70 to 80% in the second. The average bacterial count in control rooms was 66 per 100 litres of air in the E.N.T. clinic (23 tests a day for 5 days) and 324 per 100 litres in the children's playroom (17 tests a day for 6 days). The concentration of glycol in air aimed at was 0·005 mg. per litre.

A. M. M. Wilson

2350. **Bacterial Contamination of Air in Underground Trains**

R. E. O. WILLIAMS, A. HIRCH, and O. M. LIDWELL. *Lancet* [*Lancet*] **1**, 128–131, Jan. 21, 1950. 4 figs., 10 refs.

Surveys of the bacterial flora of the air by means of a special type of slit-sampler for long-period sampling were carried out in trains of the London Underground system. It was shown that even during the rush hours of the evening, when over 100 passengers crowded into each car for certain parts of the journey, the maximum total viable bacterial count in any one-minute period was only 170 per c.ft. (6,000 per c.m.) of air, with an average for one route of 47 per c.ft. (1,660 per c.m.). The streptococcal counts were extremely low; the average for the route quoted above was only 0·33 per c.ft. (11·6 per c.m.). These figures compare very favourably with the mean counts obtained in a large series of observations in elementary-school class rooms. Whenever a train stopped at a station, the movement of the passengers entering or leaving the car appeared to cause an immediate rise in the colony count, but this tended to settle very quickly soon after the train got under way—even when the car was most crowded. As would be expected, there was a steady rise in temperature of about 12° F. (6·7° C.) during each run [presumably during the long underground section] but there was no systematic change in the relative humidity.

The slit-sampler itself was housed in a driver's cab forming part of the central car of the train, and was fed with air drawn from the end of the passenger car (a " non-smoker ") by means of a fan over which was a closely fitting hood with its orifice projecting into the passenger car. Observers at each end of the car kept records of the number of passengers per section, and the temperature and humidity were measured at about 10-minute intervals on the excess air from the sampler hood. The authors appreciate the possibility that their

figures might not apply to air drawn from the centre of the car. But it is clear, within the limit of these experiments, that there was no massive accumulation of bacteria in the air of the underground trains in question.

H. J. Bensted

2351. **The Dependence of Respiratory Disease on Air Pollution in Towns.** (О зависимости болезней органов дыхания от загрязнения городского воздуха)
R. A. Babayants. Гигиена и Санитария [*Gigiena*] No. 12, 3–11, Dec., 1949. 4 figs.

The relation between air pollution in Leningrad and incidence of respiratory diseases was studied. Incidences of tonsillitis, tuberculosis of lungs, pleurisy, pneumonia, bronchitis, and diseases of the pharynx and adenoids were analysed and compared with incidences of rheumatism and diseases of the digestive tract and cardiovascular system. The latter group were taken as controls.

The incidence of the diseases in the residential part (free from industrial pollution of air) of the town was taken as a unit of comparison. Analysis showed that all the diseases in the first group are significantly commoner in the industrial part of the town. Thus tonsillitis occurs 2 to 3 times, bronchitis 3 to 5 times, pneumonia 2 to 3 times, pleurisy 3 to 4 times, and pharyngitis and adenoids 5 to 6 times more frequently in industrial than in residential areas. These findings should be further scrutinized by investigation of the influence of winds and the season of the year on the occurrence of the diseases.

In the second group (rheumatism, diseases of the digestive tract and cardiovascular system) there was no significant relation between air pollution and the incidence of the diseases.

E. W. Collis

2352. **The Single Throat Culture as an Index of the Bacterial Flora of the Respiratory Tract**
J. H. Dingle, T. J. Abernethy, G. F. Badger, J. W. Beard, N. L. Cressy, A. E. Feller, I. Gordon, A. D. Langmuir, C. H. Rammilkamp, and E. Strauss. *American Journal of Hygiene* [*Amer. J. Hyg.*] **50**, 168–174, Sept., 1949. 14 refs.

Repeated throat swabs on alternate days were taken from volunteer subjects kept in strict isolation, and the cultures examined. A special search was made for *Streptococcus pyogenes* and pneumococci, which were often present intermittently in the cultures from any one person, but not consistently, despite the unlikelihood of repeated re-infection. An analysis was made of the results of culture in 37 cases in which the first and last swabs in the series gave a positive culture of one of the above organisms, it being assumed that the organism was actually present in the throat throughout the period of examination in these cases. It was clear that, in the group studied, a single swab examined by direct plating would give a positive result in only 31% of carriers of *Strep. pyogenes*. With more selective media this figure might be raised to 67%. Similar conclusions were reached with regard to the identification of pneumococcal carriers. The authors emphasize that these figures relate only to the group of men studied, and would probably vary in repeat experiments.

Scott Thomson

2353. **Source of Two Hospital-Infected Cases of Tetanus**
S. Sevitt. *Lancet* [*Lancet*] **2**, 1075–1078, Dec. 10, 1949. 1 fig., 4 refs.

In two middle-aged patients, after open surgical operations for treatment of conditions arising out of fractures of the lower limb, clinical signs of tetanus developed. One of the cases ended fatally. Bacteriological examination of material from the wounds in both cases did not reveal the presence of *Clostridium tetani*.

It seemed possible that building reconstruction work adjacent to the theatre in which the patients underwent operation was the source of infection, since animal hair was being incorporated as a binding agent in the plaster for the walls. The animal hair was blended goat hair believed to be of Abyssinian origin.

Investigation of the ventilating system for the theatre-suite in which infection was believed to have taken place suggested that infected dust from the region where the building operations were in progress, and where the plasterers were beating out the goat hair, could readily have gained entrance to the theatre in use. Bacteriological examination failed to reveal the presence of *Cl. tetani* in the air from the theatre-suite or in the dust from the actual theatre in use, but from sweepings of the rooms under repair, the goats' hair, and the main corridor outside the operating theatre, *Cl. tetani* was recovered. The talcum powder used for powdering the surgeon's gloves was also found to be contaminated with this organism. Evidence is produced to show that the talcum powder was contaminated in the theatre-suite with tetanus-laden dust. Inadequate sterilization of packets of this contaminated talcum powder left viable *Cl. tetani*, and it seemed likely that the wounds of both patients could have been infected from this vehicle.

The inadequacy of the existing ventilating system and the method of sterilizing the talcum powder are discussed and the need for improved methods is stressed.

H. J. Bensted

2354. **The Importance of the Tuberculin Test in the Routine Examination of Children**
F. A. Heimann and D. J. Ap Simon. *Medical Officer* [*Med. Offr*] **83**, 67–69, Feb. 18, 1950. 23 refs.

The literature on the changing incidence of tuberculosis is discussed at some length and the limitations of some of the methods used are stressed. It is of the utmost importance in public health to ascertain the incidence of primary infection in children and young adults in spite of the alleged comparative unimportance of the childhood type of tuberculosis. [The abstracter cannot agree with the statement that late primary infection is in the great majority of cases equally harmless.]

The authors carried out tuberculin tests on 3,269 school children at Bournemouth over the period May, 1945, to December, 1949, and studied the relation of tuberculin reaction to radiological findings. Tuberculin jelly was employed throughout the survey. The total incidence of tuberculous infection was 18·2%. The incidence by age groups and sex is given in two tables. The results are statistically analysed. While the incidence was lowest in children under 5 (7·6%), it rose irregularly

to 25·7% in the 15 to 18 age group. The figures for girls were slightly higher than those for boys. The figures are lower than in other similar surveys carried out in predominantly industrial areas. Of the positive reactors 468 or 78·7% were radiographed. Active primary tuberculosis was found in 4·5%, necessitating sanatorium treatment. The radiograph was normal in 66·7% of the positive reactors. B.C.G. vaccination is advocated for the tuberculin-negative reactors on epidemiological grounds. *E. Nassau*

2355. **Diphtheria Immunisation in Young Babies. A Study of Some Factors Involved**
M. BARR, A. T. GLENNY, and K. J. RANDALL. *Lancet* [*Lancet*] **1**, 6–10, Jan. 7, 1950. 3 refs.

At the present time the state of immunity to diphtheria infection in the population is undergoing considerable change. On the one hand widespread immunization has raised the level of immunity in the population, on the other it has led to a sharp decline in the incidence of diphtheria, and consequently to a lack of secondary stimulation of antitoxin levels by epidemics. It is possible that general immunization will lead to a slightly inadequate level of immunity because the dose is too small (or because stimulation by epidemics is absent) and this might conceivably result in high and adequate levels in subjects responding well, but in low and inadequate antitoxin levels in subjects responding poorly.

The purpose of this investigation was to determine the best age for immunization of babies. The presence of a high level of antibodies in the circulation of infants, due to passive immunity, that is, passage of antitoxin from mother to child by the cord blood, may interfere with immunization by neutralizing the first dose of toxoid. For this reason 2 doses of 0·5 ml. alum-precipitated toxoid (A.P.T.) were given to babies at intervals of 6 weeks or more. A large first dose in babies does not cause a reaction and might overcome the neutralizing action of circulating antitoxin. The level of antitoxin at the time of immunization was determined either by direct assay from the blood or by calculation from the value obtained at birth from the cord blood.

A level of maternally derived antitoxin in the baby below 0·04 unit per ml. did not interfere with active immunization. When the level was above 0·1 unit per ml. immunization was unsatisfactory.

Immunization was successful in 20 babies aged 6 to 13 weeks at the time of the first injection; 5 of these babies were under 2 months old. When immunization was started after the age of 6 months the response was not quite so good. The antitoxin values in babies under 6 months were higher when the second injection of A.P.T. was given 10 to 18 weeks after the first than at 6 to 9 weeks after the first. This was not so in babies over 6 months. An explanation may be found in the inadequacy of the primary stimulus in relation to the higher weight and greater amount of circulating antibody in older babies.

Taking the antitoxin levels of cord blood of 200 babies born in South-East London, and calculating from these values the antitoxin levels at the age of 3 months, the authors estimate that 80% of the population could be successfully immunized at that early age. A series of 3 injections, at the ages of 3, 6, and 18 months, is suggested. The response of expectant mothers and of their babies shows no correlation. *K. S. Zinnemann*

2356. **Observations on Repeated Smallpox Vaccination of Individuals with a Previous History of Post-vaccinal Encephalitis.** (Beobachtungen bei Pockenschutz-Wiederimpfungen von Personen, die eine Erkrankung an Encephalitis post Vaccinationem durchgemacht haben)
F. PUNTIGAM and J. DAIMER. *Österreichische Zeitschrift für Kinderheilkunde* [*Öst. Z. Kinderheilk.*] **4**, 6–14, 1949. 1 fig., 4 refs.

The authors report investigations of 32 persons who had been vaccinated between the ages of 4 to 10 years and had suffered from post-vaccinal encephalitis after an incubation period of 10 to 14 days. Clinically there was a rapid onset; the cases were characterized by fever, headache, vomiting, stiffness of neck, drowsiness, pyramidal paralysis, and ocular palsies. During their military service 7 to 15 years later, 15 were re-vaccinated; in spite of their previous severe reaction they had completely recovered, and 11 were re-vaccinated once and 4 twice without any damage. According to Pette and Fanconi the demyelinating encephalo myelitis following vaccination and some acute specific fevers is the result of an antigen-antibody reaction (neuro-allergy). The reason that the 15 re-vaccinated persons did not show any ill effect was that the immunity conferred by their encephalitis had not yet subsided. *Franz Heimann*

2357. **Anopheles Eradication in Cyprus**
H. M. SHELLEY. *Medical Officer* [*Med. Offr*] **83**, 27–28, Jan. 21, 1950.

This paper gives an excellent description of a landmark in the history of man's conquest of malaria. Cyprus, at one time considered one of the most malarious parts of the world, has, in the course of 4 years, been rid of anopheline vectors, and the victory has been achieved at the cost of some £300,000, which works out at about 13*s*. per head of population. The article ends with a warm tribute to the executive officer, Mehmed Aziz, a Cypriot Turk who began his training in 1913 when Ronald Ross visted the island, and " whose genius, power of organization, and man management prove him not only a great malariologist, but also a born leader among men."
R. M. Gordon

2358. **An Attempt to Eradicate Repeated Bacterial Infections in a Family.** [In English]
A. LICHTENSTEIN and G. MELIN. *Acta Paediatrica* [*Acta paediatr., Stockh.*] Suppl. 75, 64–74, 1949. 6 refs.

A family of 3 adults and 3 children suffered from recurrent respiratory and skin infections over a period of 8 months. The trouble started when the eldest child aged 6 had measles followed by pneumonia, tonsillitis, and erythema nodosum. She was found to be a carrier of type-8 β-haemolytic streptococci, and subsequently all the members of the family, except the father, were found to be carriers of the same organism. In addition some members of the family were carriers of *Staphylococcus aureus* and type-6 pneumococci. Not only was the

respiratory tract infected, but the same bacteria were recovered from hands, clothing, and dust.

The family were treated for 8 days with penicillin in beeswax and oil, 300,000 units daily for the adults, 150,000 units for the children aged 6 and 4, and 75,000 units for the baby aged 1. The family then vacated their flat, which was thoroughly cleansed and washed with chloramine and the upper air treated with aerosol " aeryl II ". On return to the flat they all enjoyed a year of good health, and a subsequent bacteriological examination failed to reveal either streptococci or pneumococci.

N. M. Jacoby

2359. **Family Service Units for Problem Families**

D. JONES. *Eugenics Review* [*Eugen. Rev.*] **41**, 171–179, Jan., 1950.

The characteristics of a " problem family " are defined and the causes of the unsatisfactory conditions are discussed, with special comment on the complexity of the factors involved. Various modes of dealing with these unsatisfactory conditions are mentioned, while the poor results obtained are attributed to failure of the problem families to utilize the help available. The immediate effect of general social improvement is not to eradicate problem families, but to bring them into prominence as a minority who do not benefit from these measures. The failure to benefit is due to personal deficiencies which are untouched by large-scale social changes. So that the individual attention needed by each family may be given, the author suggests that they should be referred to a Family Service Unit by the other social organizations. Having no official status, the Family Service Unit acts by first gaining the friendship and co-operation of the individual members of the problem family and then assisting them to attain independence and self-respect, so that regeneration results from the family's belief in its own power of recovery. The Family Service Unit also prevents the overlapping of sometimes contradictory policies of other social bodies. The method employed is for one social worker to accept responsibility for the welfare of the family, giving practical aid with budgeting, cleaning, repairing, and disinfecting, and ensuring that the family uses existing social services, including hospital treatment, as required. Because the members of problem families are childish, immature, frightened people, all assistance has to be based upon friendly relationship.

Generalizations about the results of treatment by the Family Service Units are premature, but results so far suggest that some improvement always follows.

Three Family Service Units exist—Liverpool, London, and Manchester. Each worker, acting under the supervision of a fieldwork organizer, is responsible for 12 to 25 families at a time. Although, owing to the small numbers dealt with by each worker, the service is expensive, it is considered that, apart from humanitarian issues, economy really results. Thus, unless this service is given, the families remain a constant burden on the ratepayers and taxpayers, and its members gradually drift into institutions such as approved schools or prisons wherein they are maintained at considerable expense.

A. Michael Critchley

2360. **Methods of Measuring Results in the Treatment of Cancer**

P. STOCKS. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **1**, 187–197, Jan., 1950. 7 refs.

The four basic problems in measuring results of treatment of cancer are: (1) the initial selection of the patients for treatment; (2) the follow-up of patients; (3) the differentiation of cancer deaths from other deaths; and (4) the measurement of the proportions surviving free of cancer or escaping death from cancer. The only satisfactory solution of the selection problem is the registration and follow-up of every patient with cancer within a geographical area, with grouping according to the kind of treatment given. Meanwhile, if a rate is being based upon patients referred to a centre for treatment, those who died from cancer or whose disease had become too advanced before treatment could be started should be included. Such losses may arise from defects of organization or unavoidable delays and should therefore be included as part of the risk of accepting the treatment advised. Lack of uniformity in the stage-grouping of cases also invalidates comparisons. In comparing surgical treatment with radiotherapy the stage should be fixed before operation, and not amended as a result of operative findings. Corrections for patients lost sight of are always of doubtful validity, and the object must be to reduce the numbers until little error can result from ignoring them. Deaths from intercurrent disease should include all deaths from a cause other than cancer, whether or not cancer was present.

Statistical measures of the effectiveness of treatment may be based upon (*a*) the number of patients treated who did not die of cancer within a specified period, or (*b*) the number alive with no evidence of growth at the end of a specified period: these are quite different measures. Sometimes, in the absence of accurate information, the measure must be based upon the mere fact of the patients being alive or dead, taking the form of (*c*) the number of months of life experienced after the beginning of treatment, compared with the expected number according to a standard life table, or (*d*) the total survival rate, corrected by allowing for the probable number of deaths from other causes. A measure commonly used is the " net survival rate ", defined as " the ratio: total alive after x years/total treated *less* sum of those lost sight of and those who died with no evidence of cancer before the end of x years." But an accurate rate cannot be obtained by jumping straight to x years, and the higher the value of x, the more fallacious does the rate become. The correct method is to calculate the probability of escaping death from cancer for each separate year, starting each year afresh with the new number at risk, and finally to multiply the successive probabilities (sometimes known as the " actuarial method "). The rate for each year is given by $\left(n-h-D-\frac{E}{2}\right)/\left(n-h-\frac{E}{2}\right)$ where n=number alive at beginning of interval, h=number lost sight of in interval, D=number dying from cancer in interval, and E=number dying of intercurrent disease in interval. An alternative " cancer-free survival rate " is suggested

and illustrated. This also is calculated by the actuarial method and is free from several fallacies attaching to the present cure rates. The formula for each year is $\left(a+\frac{f}{2}\right)/(a^1-h)$ where a=the number of patients still living without cancer at the end of the year, f=the number who died during the year without cancer present, a^1=the number without cancer at the beginning of the year, and h=the number lost sight of during the year. Generally, in assessing the results of treatment, it is assumed that when division is made into stages of disease, the age of the patient is unimportant. This may be justifiable, but is not strongly founded and deserves statistical investigation. *A. Bradford Hill*

2361. **Statistical Studies of Heart Disease. V. Illness from Heart and Other Cardiovascular-renal Diseases Recorded in General Morbidity Surveys of Families**
S. D. COLLINS. *Public Health Reports, Washington* [*Publ. Hlth Rep., Wash.*] **64**, 1439–1492, Nov. 18, 1949. 13 figs., 24 refs.

EPIDEMIOLOGY

2362. **The Increased Poliomyelitis Incidence in the Higher Age-groups and its Causes.** (Den i högre åldrar ökade poliomyelitmorbiditeten och dess orsaker)
W. WERNSTEDT. *Nordisk Medicin* [*Nord. Med.*] **41**, 361–363, Feb. 25, 1949. 3 figs.

The recent change in the age distribution of poliomyelitis has been as obvious in Sweden as elsewhere, and is shown by a comparison between the author's figures for the epidemic in Sweden in 1911–1913 (2,660 cases) and those of Olin and Heinerz for 1930–1939 (2,299 cases). In 1911 the maximum incidence was in children under 6, falling rapidly thereafter. In 1939 the incidence was much the same at all ages up to 25, with a shallow maximum between 10 and 15 years of age. As a reason for this, changes in the nature of the virus have been postulated but the author suggests that this is merely an expression of ignorance.

Before 1911 epidemics did the most damage in the rural areas, where total morbidity was higher and there was a higher incidence of morbidity in the older groups than in the towns. The author found that the morbidity rates were *inversely* proportional to the population density, and these findings in an epidemic period were confirmed by Olin and Heinertz between 1930 and 1939. Further, the author had noted that areas where there was an epidemic one year were relatively free the next.

The knowledge that non-paralytic and asymptomatic infections occur, the presence of antibodies in adult sera (higher in town dwellers), and the occurrence of sporadic cases between epidemics justify the belief that active immunization is always going on. This natural immunization occurs later and is less thorough—and hence epidemics are more severe—where the population is thinnest and social contacts are least frequent.

The author suggests that the shift in the age incidence of poliomyelitis is really a social phenomenon due to the increased numbers of older children and young adults who are brought up in the country, where contacts are few and natural immunization is weak, and who then come to live, study, or work in the towns where the chance of contact with the virus is greatly increased.
A. M. M. Wilson

2363. **Relative Familial Attack Rates as a Measure of Pathogenicity of an Organism; Organisms Associated with Diarrheal Disease**
J. WATT and M. WALTON. *American Journal of Hygiene* [*Amer. J. Hyg.*] **50**, 263–269, Nov., 1949. 5 figs.

Samples of faeces from a very large number of children under 10 years were examined for pathogens at monthly intervals. When a pathogen was isolated the family was visited and inquiries were made about the incidence of diarrhoea in other members of the family during the preceding month, 691 children being included in the report. Infection by *Shigella flexneri* was found in 212, *Shig. sonnei* in 130, salmonella in 66, and *Shig. alkalescens* in 78, the remaining 205 cases being controls. Approximately twice as much diarrhoea was reported in families containing children infected by known pathogens as in the control families and this ratio did not vary appreciably with the organism. Families from which *Shig. alkalescens* was isolated had an attack rate similar to that found in the control group. *Scott Thomson*

2364. **The Infectiousness and Incubation Period of Primary Atypical Pneumonia**
W. S. JORDAN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **50**, 315–330, Nov., 1949. 8 figs., 49 refs.

Of 67 cases of primary atypical pneumonia there was a history in 29 (representing 25 families) of similar illnesses in family contacts. A large proportion of the people in these families had respiratory illnesses, and one-half of these illnesses were believed to be atypical pneumonia. The average incubation period was $12\frac{1}{2}$ days.
Scott Thomson

2365. **Pemphigus Neonatorum in Maternity Hospitals. An Epidemiological Study.** [In English]
G. MELIN and G. WALLMARK. *Acta Paediatrica* [*Acta paediatr., Stockh.*] Suppl. 75, 175–186, 1949. 15 refs.

In a small outbreak of pemphigus neonatorum, pathogenic staphylococci were found on the hands and clothes and in the noses and throats of a high proportion of the infants, staff, and mothers. They were also present in the dust and air of the nursery. Incidentally, they were also found in almost the same degree in a nursery where the infants were not affected. The authors consider that infection is spread by both adults and infants.
N. M. Jacoby

2366. **Influenza. A Study of Two Outbreaks**
C. M. OGILVIE, R. H. M. MAVOR, and C. WEYMES. *British Medical Journal* [*Brit. med. J.*] **1**, 269–271, Feb. 4, 1950. 1 fig., 3 refs.

Between January 15 and February 22, 1949, outbreaks of virus-A influenza occurred at two military training establishments in the Highlands of Scotland. In unit A the attack rate was 6% and in unit B it was 14%. Recruits and seasoned men were equally affected. There was

definite evidence of infection with virus A in 6 cases, in 5 of which there was an antibody rise against the PR8 strain and in the sixth only against the then current Continental strain (A/Paris PL1/49). Recruits and seasoned men were equally affected and it is suggested that this indicates that the communities had had no recent experience of the infecting agent. Exposure to cold seemed to play a greater part than cross-infection in determining the incidence of the disease.

A. H. Gale

INDUSTRIAL MEDICINE

2367. **Industrial Efficiency as Affected by Food Intake During Mid-morning and Mid-afternoon Rest Periods**
J. HALDI and W. WYNN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 268–273, Nov., 1949. 5 refs.

The common inclination of workers to stop work in the mid-morning and mid-afternoon and to take food or drink may be due to a physiological need for food or to a psychological need for a restful change from monotony. The efficiency of women working all day at top speed sewing cotton bags was therefore studied in relation to the kind and amount of food taken at mid-morning and mid-afternoon rest periods. All workers sewed at top speed because they were paid according to the number of bags sewn.

The rest periods were of 15 minutes, and during a period of 3 weeks the workers received at this time either: (1) sausage, chips, bun, and soft drink (650 Calories); or (2) cake, banana, milk (300 Calories); or (3) milk chocolate (150 Calories); or (4) soft drink (80 Calories). On 2 days they were given nothing. The differences in output on various days were not statistically significant. It is therefore inferred that such supplements are not required as far as provision of energy is concerned. It is, however, pointed out that the workers were by no means pleased at being allowed no food or drink on the two control days, and it is therefore thought advisable to allow workers a wide choice of food or drink during rest periods. *S. S. B. Gilder*

2368. **The Significance of Rhythm in Work in Hot Shops.** (Значение микроритма при работе в горячих цехах)
A. A. ARKADYEVSKII. Гигиена и Санитария [*Gigiena*] No. 12, 24–28, Dec., 1949. 3 figs.

Investigations were carried out at a steel-rolling mill to assess the dependence of the productivity of the workers on their physical fatigue. The former was estimated by the time required by individual workers for the various parts of the procedure—this is called the rhythm of the work; the latter was assessed by the temperature and pulse rate of the worker. The selected group of 12 workers were of approximately the same age and had had the same industrial experience; 500 observations were made on each individual worker under investigation.

It was found that the 12 workers could be divided into four groups with reference to productivity as measured by the time requirement for the various parts of the steel-rolling process. The group of workers with the longest time requirement showed also the highest degree of fatigue. This was particularly noticeable in the afternoon. Further analysis of the various parts of the procedure showed that it was the setting of the steel product in the narrow, right-angled hole of the rolling table which gave rise to such great individual differences. It is suggested that the rectangular shape of the apertures should be replaced by a conical one, and that 20 minutes' rest is required for every 10 minutes of work. These improvements, it is expected, will bring about the reduction of the individual time requirement, improve the so-called work rhythm, and reduce fatigue in the workers irrespective of their individual skill.

E. W. Collis

2369. **Pneumoconiosis after Exposure to Sulphur Dioxide Fumes and Dust from Coke Fires**
L. DUNNER, R. HARDY, and D. J. T. BAGNALL. *Lancet* [*Lancet*] **2**, 1214–1216, Dec. 31, 1949. 4 figs., 12 refs.

Abnormalities were found in the radiographs of the lungs of 10 out of 50 to 60 men attending a chest clinic between 1941 and 1949 whose work involved exposure to sulphurous fumes from coke fires—boiler-stokers, blacksmiths, platers, and men employed at coke-ovens and gas-works. All 10 patients complained of respiratory symptoms, the chief of which were productive cough, dyspnoea on exertion, and irritation of the nose and throat. The severity and duration of their symptoms bore no direct relation to the duration of exposure to the fumes or to the extent of the *x*-ray abnormality. Radiography showed irregular patchy fibrosis involving both lungs, but usually one much more than the other. In most cases the mid- and lower zones showed nodulation, occasionally becoming confluent and producing patchy consolidation. Emphysema was usually present. The fine fraction of a sample of coke-flue dust obtained by a coke-oven worker contained 34% total silica, 2·1% free silica, and 17·5% iron compounds (expressed as Fe_2O_3). The authors conclude that the cases in this series are examples of an occupational pulmonary disease, and suggest that protracted exposure to sulphur dioxide causes localized chronic inflammation in the lungs, with accumulation of siliceous dust in the affected areas.

[Four radiographs are reproduced, but too poorly to be useful. A good deal of confirmatory evidence will be necessary before this type of industrial exposure can be taken as producing a new form of pneumoconiosis. Sulphur dioxide has been claimed by previous authors to play a part in industrial lung diseases, and has been used in animal experiments (often in combination with oxides of nitrogen) as an adjuvant or accelerator in studying the effects of particulate matter introduced into the lungs.] *H. E. Harding*

2370. **Arsine Poisoning in Industry. Report of a Case**
M. STEEL and D. V. G. FELTHAM. *Lancet* [*Lancet*] **1**, 168–110, Jan. 21, 1950. 28 refs.

2371. **Occupational Leukoderma. A Report of Six Cases Observed in a South African Factory**
R. J. J. LOCKHART and L. J. A. LOEWENTHAL. *South African Medical Journal* [*S. Afr. med. J.*] **23**, 867–868, Oct. 22, 1949. 2 figs., 8 refs.

Physiology and Biochemistry

2372. **Micro-Determination of Blood Iodine**
J. W. DECKER. *Harper Hospital Bulletin* [*Harper Hosp. Bull.*] 7, 321–322, Nov.–Dec., 1949. 4 refs.

Using the original method of Salter *et al.* (*Endocrinology*, 1944, **35**, 380; *J. Pharmacol.*, 1944, **81**, 331), modified in that sodium hydroxide was used as a serum-digestion medium, the author determined the protein-bound iodine content of the serum of 200 patients, of whom 43 were suffering from various types of thyroid disease.

The values found in hyperthyroidism (15 cases) were 3·5 to 10·1 μg. per 100 ml. (mean 6 μg.), in hypothyroidism (12 cases) 0·4 to 2·8 μg. per 100 ml. (mean 1·6 μg.), and in euthyroidism (16 cases) 1·2 to 4·2 μg. per 100 ml. (mean 2·9 μg.). From these results the author suggests that values indicating hypothyroidism range from 0 to 2 μg. protein-bound iodine per 100 ml., those indicating euthyroidism from 2 to 4 μg., and those indicating hyperthyroidism from 4 μg. upwards.

Malcolm Woodbine

2373. **Properties of the Acid Phosphatases of Erythrocytes and of the Human Prostate Gland**
M. A. M. ABUL-FADL and E. J. KING. *Biochemical Journal* [*Biochem. J.*] **45**, 51–60, 1949. 4 figs., 25 refs.

2374. **Effect of Cortical Stimulation on Respiratory Rate**
T. J. SPEAKMAN and B. P. BABKIN. *American Journal of Physiology* [*Amer. J. Physiol.*] **159**, 239–246, Nov., 1949. 4 figs., 10 refs.

2375. **Hemoglobin Concentration and Physical Fitness**
H. CULLUMBINE. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 274–277, Nov., 1949. 8 refs.

The coefficients of correlation between the blood hemoglobin concentration and the responses to various exercise tests have been calculated for Ceylonese subjects aged 10 to 20 years. It is concluded that the blood hemoglobin concentration is correlated significantly with speed of movement, strength and the ability to sustain prolonged moderate muscular effort. There is no evidence for a significant correlation between the hemoglobin level and either the response to moderate exercise or the response to severe exercise.—[Author's summary.]

2376. **Relationship between Resting Pulse Rate, Blood Pressure and Physical Fitness**
H. CULLUMBINE. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 278–282, Nov., 1949. 9 refs.

One thousand Ceylonese subjects, aged 10 to 25 years and of both sexes, performed a series of exercise tests. It has been concluded that the slower the resting pulse rate or the lower the resting systolic blood pressure, the slower is the post-exercise pulse rate or the lower is the post-exercise systolic blood pressure, respectively. Speed of movement, strength and the ability to sustain moderate exercise are positively correlated with the resting systolic blood pressure.—[Author's summary.]

2377. **Immunochemical Studies on Blood Groups. The Preparation of Blood Group A and B Substances and an Inactive Substance from Individual Horse Stomachs and of Blood Group B Substance from Human Saliva**
H. BAER, E. A. KABAT, and V. KNAUB. *Journal of Experimental Medicine* [*J. exp. Med.*] **91**, 105–114, Jan., 1950. 21 refs.

Blood-group substances were isolated from saliva of persons of blood group B, and from the mucosa of individual horse stomachs. For the latter the following method was used: The mucosal linings of individual horse stomachs were dehydrated with alcohol, dried *in vacuo*, and stored frozen. They were then digested with pepsin at *p*H 2, a further quantity of pepsin being added after 5 days and digestion then continued for a further 5 days. The digested linings were then dialysed against 3 changes of distilled water, the *p*H was readjusted to 2, and the materials redigested with pepsin. The *p*H was then raised to 4 with sodium acetate, and the digest was mixed with 5 volumes of alcohol; the precipitate was collected, centrifuged off, and dried over phosphorus pentoxide, then soaked and extracted with successive quantities of water. The solutions were reprecipitated with sodium acetate and alcohol, the procedure being repeated if necessary. The product so obtained was extracted overnight with 90% phenol and centrifuged; after repetitions the supernatants were fractionally precipitated with alcohol–phenol to a final concentration of 15% alcohol; the precipitates were extracted with phenol, and reprecipitated at 25% alcohol. The phenol was removed by repeated washing with alcohol, and the precipitates dried, dissolved in water, reprecipitated with sodium acetate and alcohol, washed with alcohol, and dried.

The properties of the human blood-group substances resembled those of human and hog blood-group substances previously isolated, but those from horses had a lower content of hexosamine and reducing sugar, and a higher total and non-hexosamine nitrogen, than materials from the other species did. Individual horse stomachs showed A or B activity or both, but certain stomachs yielded substances of chemical composition similar to that of the blood-group substances, but not possessing A, B, or O activity, as measured by their capacity to inhibit isoagglutination. Fucose has been identified as a constituent of the horse blood-group substances by paper chromatography.

C. L. Oakley

2378. **Sources of Error in Oximetry**
J. O. ELAM, J. F. NEVILLE, W. SLEATOR, and W. N. ELAM. *Annals of Surgery* [*Ann. Surg.*] **130**, 755–773, Oct., 1949. 10 figs., 27 refs.

2379. **Sequences in the Formation of Clots from Purified Bovine Fibrinogen and Thrombin: A Study with the Electron Microscope**
K. R. PORTER and C. VAN ZANDT HAWN. *Journal of Experimental Medicine* [*J. exp. Med.*] **90**, 225–232, Sept., 1949. 11 refs.

The authors describe the morphological features of the clotting processes as observed by means of the electron microscope. The sequence of changes observed during the formation of clots from purified bovine fibrinogen and fibrin are described in detail. The formation of crystal-like structures was a striking feature of the process. They conclude that fibrinogen molecules are polymerized by the action of thrombin to form needle-shaped, crystal-like protofibrils which then become aligned into fibre strands by lateral association. The identity of these crystal-like fibres is maintained within the compound fibre strands.

They suggest a model of the fibrinogen molecule, based on their observations, which may satisfy the reported physical constants and data from *x*-ray diffraction studies. *R. Winston Evans*

2380. **The Chain Reaction of the Blood Clotting Mechanism in Relation to the Theory of Hemostasis and Thrombosis**
J. H. MILSTONE. *Blood* [*Blood*] **4**, 1290–1297, Dec., 1949. 1 fig., 25 refs.

2381. **The Coagulation Mechanism. With Specific Reference to the Interpretation of Prothrombin Time and a Consideration of the Prothrombin Consumption Time**
A. J. QUICK. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 1016–1023, Nov., 1949. 1 fig., 12 refs.

2382. **The Morphology of Thrombocytes as Shown by the Electron Microscope.** (Zur Morphologie der Thrombozyten im Elektronenmikroskop)
H. BRAUNSTEINER. *Wiener Zeitschrift für Innere Medizin* [*Wien. Z. inn. Med.*] **30**, 448–451, Nov., 1949. 7 figs., 4 refs.

2383. **Quantitative Observations on Vascular Reactions in Human Digits in Response to Local Cooling**
H. H. WOLFF and E. POCHIN. *Clinical Science* [*Clin. Sci.*] **8**, 145–154, 1949. 6 figs., 3 refs.

Quantitative studies on the vasodilator after-reactions in recently cooled fingers show that the magnitude of these reactions increases as the cooling temperature is lowered and with the duration of cooling. The after-reactions may be delayed as much as 2 hours or longer, depending on the subject's general and local vasomotor tone, and may persist for as long as 2 to 3 hours. Circulatory arrest during or after exposure to cold does not alter the size of the subsequent after-reaction. These observations are consistent with the view that the after-reaction is caused by chemical substances liberated during cooling as a result of tissue injury. They suggest also that the substances are both stable and fixed in the tissues.
R. T. Grant

2384. **Parenteral Nutrition. X. Observations on the Use of a Fat Emulsion for Intravenous Nutrition in Man**
S. W. GORENS, R. P. GEYER, LeR. W. MATTHEWS, and F. J. STARE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 1627–1633, Dec., 1949. 3 figs., 7 refs.

Eleven patients received intravenous injections of an emulsion consisting of 15% coconut oil, 4·3% dextrose, 0·5% soya bean phosphatide, and 1% polyglycerol esters. The size of the emulsion particles was mainly less than 1μ and did not exceed 3μ. This emulsion furnished 1,600 Calories per litre. The re-establishment of a positive nitrogen and potassium balance was demonstrated in one case. In 2 patients the emulsion was given in a daily dosage of 6 and 4 g. of fat per kg. body weight for 11 and 26 days respectively; in one of these cases two-thirds of the total calories were supplied intravenously for 7 days. Weight loss was prevented by the intravenous alimentation. Necropsy on 3 of the patients revealed no pathological changes. In 3 of the patients pyrexia developed which was attributed to the development of pyrogens in the emulsion.
A. C. Frazer

2385. **The Nutritional Effects of Heat on Food Proteins with Particular Reference to Commercial Processing and Home Cooking**
H. H. MITCHELL, T. S. HAMILTON, and J. R. BEADLES. *Journal of Nutrition* [*J. Nutrit.*] **39**, 413–425, Nov. 10, 1949. 12 refs.

By studying nitrogen balance and growth in rats, the nutritional value of the proteins of various foods was compared before and after they had been subjected to heat during commercial processing and home cooking. Both the digestibility and the biological value of the proteins were decreased in corn, peanut meal, sunflower-seed flour and cotton-seed flour. There was no change in the nutritional value of beef proteins after roasting, while heating improved the nutritional value and digestibility of the protein of linseed. All the heat processes studied reduced the amount of aneurin in the foods, but did not affect the unbound pantothenic acid.
J. Yudkin

2386. **The Role and Sources of Vitamin B_{12}**
A. M. HARTMAN, L. P. DRYDEN, and C. A. CARY. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] **25**, 929–933, Nov., 1949. 4 figs., 4 refs.

2387. **Nitrogen Balance in Men Consuming Raw or Heated Egg White as a Supplemental Source of Dietary Protein**
H. H. SCUDAMORE, G. R. MORELY, C. F. CONSOLAZIO, G. H. BERRYMAN, L. E. GORDON, H, D. LIGHTBODY, and H. L. F. EVOLD. *Journal of Nutrition* [*J. Nutrit.*] **39**, 555–565, Dec. 10, 1949. 22 refs.

Unheated egg white contains a protein, ovomucoid, which strongly inhibits the activity of trypsin *in vitro*; this anti-tryptic effect is destroyed by heating, though less by dry than by wet heating. Commercially dried egg white retains much of its anti-tryptic activity. The investigation reported in this paper was designed to

determine whether the anti-tryptic properties *in vitro* of commercially dried egg white affect its digestibility *in vivo*. Two young men were the subjects of the study. They were given a controlled diet to which was added, for five successive periods, unheated lactalbumin, unheated egg white, heated egg white, heated egg white with added ovomucoid, and again lactalbumin. Clinical and biochemical examination of the subjects showed no significant changes in weight, haemoglobin level, blood count, serum protein, cholesterol, and non-protein nitrogen content, and blood pressure. Studies of nitrogen retention showed that the unheated egg white was only slightly inferior to the heated form as a source of protein, and that both were better than lactalbumin. The ovomucoid had no unfavourable effect. These results show that diminished digestibility *in vitro* does not necessarily indicate diminished digestibility (physiological availability or utilization) *in vivo*. *J. Yudkin*

2388. **Disturbances of Sensation Occasioned by Experimental Arrest of Blood Flow.** [In English]
A. AUERSPERG, O. AIDAR, and E. A. ERHART. *Arquivos de Neuro-Psiquiatria* [*Arch. Neuro-psiquiat., S. Paulo*] **7**, 371–392, Dec., 1949. 36 refs.

Disturbances of sensation in the hand were studied during and after arrest of the circulation to the upper limb. No new facts are presented. *P. W. Nathan*

2389. **The Afferent Paths and Thalamic Nuclei of the Cerebral Motor System. I. Brachium Conjunctivum and Fasciculus Thalamicus. II. Further Paths from the Pallidum, Red Nucleus, and Vestibular System to the Thalamus.** (Über die afferenten Bahnen und Thalamuskerne des motorischen Systems des Grosshirns. I. Bindearm und Fasciculus thalamicus. II. Weitere Bahnen aus Pallidum, Ruber, vestibulärem System zum Thalamus; Übersicht und Besprechung der Ergebnisse)
R. HASSLER. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **182**, 759–785, and 786–818, 1949. 36 figs., bibliography.

2390. **Experimental Observations on the Effects of a High Rate of Climb on the Human Organism.** (Observations expérimentales relatives aux effets des vitesses ascensionnelles rapides sur l'organisme de l'aviateur)
E. EVRARD. *Bruxelles-Médical* [*Brux.-méd.*] **29**, 3629–3657 and 3689–3706, Dec. 18 and 25, 1949. 7 figs., 23 refs.

The effect on man of decompression to a simulated altitude of 33,000 feet (10,000 m.) at an average rate of 143 feet (44 m.) per second has been examined. Observations were made in particular on (1) the effect of gaseous dilatation, and (2) the effect of air embolism. The effect was noted of gaseous dilatation on the middle ear, sinuses, alimentary tract, and respiratory system. Figures are given for vital capacity and alveolar-air composition. The effect on the cardiovascular system was examined from the point of view of pulse rate, blood pressure, vasomotor changes, electrocardiography, blood count, and urinary output. The effect of precipitation of dissolved gases is dealt with relatively briefly.

With regard to subjective and psychic symptoms, a mental excitability followed or accompanied by lethargy was constantly observed in the three subjects after decompression runs. It is suggested that the degree of psychic tension may be a contributory factor in the production of air embolism. The relative merits of pressurization at 2 and 3 lb. per sq. in. (0·14 and 0·21 kg. per sq. cm.) are discussed. *T. C. D. Whiteside*

2391. **Hearing of Airline Pilots. A Ten-year Study**
K. M. SIMONTON. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **20**, 418–429, Dec., 1949. 11 figs., 13 refs.

Over a period of 10 years, the hearing of 47 civil-airline pilots was tested periodically by threshold audiometry. The author admits that the tests were carried out under conditions in which not inconsiderable errors could occur. Significant average loss of hearing was found only at frequencies of 4,096 and 11,584 cycles per second; at 4,096 cycles the average loss was 10·3 decibels, and at this frequency a loss exceeding 25 decibels was found in 14 ears. Loss of hearing was in some individuals unilateral. Analysis of the results suggested that pilots whose initial audiogram showed a descending curve in the high-tone frequencies were more liable to have greater subsequent loss of hearing than those with other types of audiogram.

As changes in hearing over the 512- to 2,048-cycle frequency range were insignificant, the author concludes that loss of hearing due to flight is not a very serious problem.

[The author's findings hardly justify this conclusion unless individual results be rejected in favour of averages, and changes outside the 512- to 2,084-cycle range be ignored. Moreover, the results of audiometry are suspect; although the subjects were 10 years older, hearing at 11,584 cycles per second was better at the end than at the beginning of the period in 26 out of 94 ears.]
T. A. Clarke

2392. **Haematological Investigations in High-altitude Flight. The Haemotoxic Role of Oxygen.** (Recherches hématologiques sur les aviateurs à haute altitude. Le rôle hématoxique de l'oxygène)
M. FAVE and G. RINGENBACH. *Journal de Médecine de Bordeaux* [*J. Méd. Bordeaux*] **126**, 544–550, Nov., 1949.

The authors investigated the variations in erythrocyte count occurring in French aircrew in the course of, and after, 5 flights at 6,000 to 8,000 metres ranging from $2\frac{3}{4}$ hours to $4\frac{3}{4}$ hours in duration. Increasing concentrations of oxygen were breathed with increasing altitude above 3,000 metres. A fall in the erythrocyte count of 600,000 to 800,000 per c.mm. in 2 to 3 hours after starting to breathe oxygen was observed. A further fall of 1,200,000 to 2,200,000 per c.mm. in the next 4 days was followed by return to normal in 7 to 19 days. A similar fall in erythrocyte count was found after breathing oxygen at sea level. It is concluded that the fall in erythrocyte count was due to the increased partial pressure of oxygen in the inspired air. *N. C. Hughes Jones*

Pharmacology and Therapeutics

2393. **Influence of Curarising Agents on Cerebral Electrical Activity of the Rabbit.** (L'influence des curarisants sur l'activité électrique cérébrale du lapin)
D. QUIVY, I. BERTRAND, and T. GAYET-HALLION. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **81**, 121–127, 1950. 3 figs., 13 refs.

Changes were observed in the electroencephalogram in unanaesthetized rabbits, without artificial respiration, after the intravenous injection of various curarizing agents. When D-tubocurarine chloride or " intocostrin " was injected in a dose which killed about one-half of the animals (0·25 mg. per kg. body weight), slow alpha waves appeared, and occasionally much more rapid waves of high potential were also seen. Beta waves mainly disappeared. On intravenous injection of " 3697 RP ", (the tri-iodoethylate of tri(dimethylaminoethyloxy)-1 : 2 : 3-benzene) in a non-lethal dose (0·65 mg. per kg.) to 10 rabbits, the beta waves disappeared in all but one animal, the effect disappearing after 40 minutes. " Myanesin ", not strictly a curarizing agent, did not affect the beta waves, but a slow alpha rhythm appeared, the electroencephalogram resembling that in hypnotic sleep. *Derek R. Wood*

2394. **Antipyretic Action of Cryogenine**
G. BOURNE. *Lancet* [*Lancet*] **2**, 1126–1128, Dec. 17, 1949. 5 figs., 14 refs.

" Cryogenine ", or phenylsemicarbazide ($C_6H_5NH.NH.CONH_2$), was first employed as an antipyretic by Lumière and Chevrotier (*C. R. Acad. Sci.*, 1902, **135**, 187). White crystalline powder, a solubility of 1 in 100 in water and 1 in 25 in 90% alcohol, the compound is comparatively non-toxic when given in a dosage ranging from 24 to 40 gr. (1·5 to 2·5 g.) daily. Occasionally it causes vomiting and profuse sweating. Haemoglobinuria was noted in one instance, and a miliary rash has also been observed.

Recollecting a case of lymphadenoma in which the administration of cryogenine produced a pronounced reduction in temperature, the author decided to investigate the action of the drug in a series of 5 cases. The first patient was a man, aged 56 years, with the signs and symptoms of lymphatic leukaemia, but with lesions resembling histologically those of a systematized reticulosis. Treatment with cryogenine, 10 gr. (0·65 g.) thrice daily for 3 days, reduced the temperature to subnormal and gave transient relief from the symptoms associated with high fever. The treatment also brought about a fall in temperature in cases of rheumatoid arthritis, lymphosarcoma, carcinoma of the bronchus, and miliary tuberculosis. The patient suffering from tuberculosis was a young woman with pyrexia up to 104° F. (40° C.). During a course of 7½ gr. (0·5 g.) cryogenine, thrice daily for 1 week, the temperature was below 99·4° F. (37·4° C.). Three days after the end of the antipyretic treatment there was a rise in temperature to 100° F. (37·8° C.), but a second course of the drug again brought transient relief from pyrexia. Thus, in contrast with the other cases, the fall in temperature did not persist after the course of cryogenine therapy was terminated. The author believes that cryogenine exerts an action on the heat-regulating centre. By diminishing fever, the drug is of value in combating ill effects such as dehydration, sleeplessness, and exhaustion.
A. Garland

2395. **Failure of Oral Antipyretic Drugs to Alter Normal Human Pain Thresholds**
R. R. SONNENSCHEIN and A. C. IVY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 308–313, Nov., 1949. 20 refs.

Two methods were used for measuring the threshold to pain. In the first, the pulp of the tooth was stimulated through a metal filling with a highly damped sinusoidal current. Impulses were delivered at the approximate rate of one per second, and the intensities of the current used were measured to the nearest 0·05 volt. Two thresholds were measured by this method. The first was that for appearance of a non-painful sensation, and the second that for appearance of a painful sensation. In the second method, the pain threshold of the skin of the pad of the middle finger or of the flexor surface of the wrist was tested by a radiant heat stimulus. Exposures were limited to 4 seconds and were repeated every 2 seconds. The intensity of the heat could be varied and the appearance of pain at the end of the 4-second exposure indicated the threshold.

The effects of lactose, aspirin, amidopyrine, acetanilide, and phenacetin were tested by the first method, all the possible sources of error being well controlled. A slight but significant increase in both thresholds was found with the antipyretics and with the lactose. There was no significant difference between the effects of the antipyretics and the lactose, a fact which was confirmed by using lactose and aspirin in the second method.

It was concluded that any effect which the antipyretics have on the normal human pain threshold is a placebo effect due to suggestibility. *P. A. Nasmyth*

2396. **Some Aspects of the Pharmacology of Morphine, with Special Reference to its Antagonism by 5-Amino-Acridine and Other Chemically Related Compounds**
F. H. SHAW and G. BENTLEY. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 868–874, Dec. 17, 1949. 17 refs.

5-Aminoacridine hydrochloride (aminacrine, *B.P.*), in a dose of 5 to 10 mg. per kg., has a profound analeptic action on dogs narcotized with morphine but no action on dogs narcotized with barbiturates. A similar type

and degree of activity is shown by two closely-related substances, 4-aminoquinoline and 1 : 2 : 3 : 4-tetrahydro-5-aminoacridine, whereas 2 : 5-diamino-7-ethoxyacridine (" rivanol ") is somewhat less active. Pronounced respiratory stimulation is shown by all except rivanol. A clinical trial of aminacrine, rivanol, or neostigmine is recommended in cases of severe morphine poisoning.

These analeptic substances were investigated pharmacologically in the cat, rabbit, rat, and mouse and the results are discussed in relation to the essentially diphasic (depressant-excitant) action of morphine.

[" 5-(Ethyl-amino)-acridine ", mentioned several times in this paper, appears to be 5- (β-amino)-ethylacridine, a very different substance. The statement that " the linking of this drug (aminacrine) to the heart-muscle is not of an ionic nature, but the action is due simply to adsorption on to the heart " is self-contradictory: the adsorption of kations on muscle would at least involve ionic bonds and, in the case of aminacrine, possibly other kinds of bond as well.] *A. Albert*

2397. **1-Methyl-4-*m*-hydroxyphenylpiperidine-4-ethylketone (" Cliradon "), a New Synthetic Analgesic with Morphine-like Action.** (1-Methyl-4-*m*-oxyphenyl-piperidin-4-äthylketon (Cliradon), ein neues synthetisches Analgeticum mit morphinähnlicher Wirkung)
F. Gross and R. Meier. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 1154–1159, Dec. 3, 1949. 6 figs., 26 refs.

The pharmacological properties of the synthetic analgesic " cliradon " (1-methyl-4-*m*-hydroxyphenyl-piperidine-4-ethylketone) are described. Chemically and pharmacologically it resembles morphine and its derivatives.

The analgesic properties were tested on a variety of animals. Reduction or abolition of the pain response to a thermal stimulus (mouse tail) or to a mechanical stimulus (cat ear) were used for assay. Ten mice were tested simultaneously and reaction times were checked at 15-minute intervals; 0·5 mg. of cliradon per kg. had definite analgesic action, which increased in intensity and duration with increasing dosage. The drug appears to have greater activity than morphine. In cats also 0·5 mg. per kg. had a greater analgesic action than an equal dose of morphine. In the dog, 0·1 mg. per kg. was effective and had a sedative action.

The corresponding methylketone and propylketone also possess analgesic properties although to a lesser degree than cliradon. They are, however, less toxic.

The toxicity of cliradon varies for different species. Rabbits can tolerate large doses of the drug as well as of morphine, while the cat is very sensitive to both drugs.

The isolated frog heart will stop in diastole when the drug is perfused in a concentration of 10^{-3}. In the intact mammal there is an initial rise in blood pressure followed by a fall. This is accompanied by bradycardia. Atropine or procaine administration or vagotomy will abolish the bradycardia. It is suggested that the drug acts on the vagus via the central nervous system. Coronary circulation is increased by the drug, but no action could be demonstrated on other vessels.

Cliradon, like morphine, has a depressant action on respiration, affecting the rate as well as the respiratory volume. Respiratory stimulants will temporarily counteract the depression in animals without influencing the analgesia. Here again the site of action is the central nervous system and vagus. In the isolated gut cliradon will reduce muscle tone and height of contraction. *In situ* this reduction only occurs with large doses and is of short duration. In its anti-inflammatory reaction and power of reducing body temperature cliradon resembles morphine. *Vera N. Warren*

2398. **Clinical Experience with " Cliradon ", a New Synthetic Analgesic.** (Klinische Erfahrungen mit Cliradon, einem neuen synthetischen Analgeticum)
A. Bernstein. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 1159–1162, Dec. 3, 1949. 8 refs.

Clinical trials with the new synthetic analgesic " cliradon " (1-methyl-4-*m*-hydroxyphenylpiperidine-4-ethylketone) are described.

Out of 161 patients suffering from a variety of acute and chronic painful conditions, parenteral as well as oral administration of the drug resulted in complete relief of pain in 116 cases, partial relief in 39, and a poor response in only 6 cases. A dose of 25 mg. given subcutaneously to 2 patients caused unpleasant side-reactions such as vomiting or drowsiness. With a 10-mg. dose side-reactions were rarely seen although the dose was sufficient to give complete relief from pain for 4 to 6 hours. A good analgesic action was also obtained with 6·25 and 5 mg. and no side-reactions occurred. The analgesic action of 0·005 g. to 0·01 g. cliradon per dose corresponds to that of 0·01 g. morphine. Five to 10 mg. is therefore a suitable single dose to be given by mouth or subcutaneous injection. Increasing the dose does not improve the analgesic action, but does lead to side-reactions.

After oral administration of the drug analgesic action sets in after 20 to 30 minutes, and after subcutaneous injection within 10 to 20 minutes. No action on blood pressure, heart rate, or pulse was noticed. Respiration was affected only in patients suffering from cardiac insufficiency.

No toxic symptoms were seen after repeated administration of 5 to 10 mg. within 24 hours or when the preparation was given for periods of several weeks. There is no clear evidence of habit-formation with the drug.
Vera N. Warren

2399. **New Analgesics. II. A Clinical Appraisal of the Narcotic Power of Methadone and its Isomers. III. A Comparison of the Side Effects of Morphine, Methadone and Methadone's Isomers in Man**
J. E. Denton and H. K. Beecher. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 1146–1153, Dec. 17, 1949. 2 figs., 3 refs.

These two accounts are intended to illustrate the application of the methods used in the clinical evaluation of new analgesics, as described in Part I of this series. Tests were made on 429 patients after intra-abdom-

inal, intrathoracic, or peripheral operations to determine the analgesic power of methadone and three of its isomers in comparison with that of morphine sulphate. The DL-, L-, DL-*iso*, and L-*iso* forms were studied. The basis for comparison of the analgesic effect was an arbitrarily chosen standard dose termed the " AD 90 per cent.", which was defined as the analgesic dose giving moderate to complete relief of pain in 90% of the trials. This value for morphine, DL-methadone, and L-*iso*methadone was 7 to 9 mg. per 68 kg. body weight, that for L-methadone 4 to 6 mg., and that for DL-*iso*methadone 26 to 30 mg. An accurate estimate of the relative incidence of side-effects of morphine and the methadones proved impossible in these cases, since it was difficult to differentiate between the side-effects of the drugs and the after-effects of anaesthesia and surgery.

The comparison of the side-effects was therefore carried out on two groups of healthy volunteer subjects. The drugs were given subcutaneously at weekly intervals until all had been administered once to each subject. Before and during 5 hours after each injection, the incidence and duration of symptoms and signs, the respiratory rate, the pulse rate, and the blood pressure were recorded. The Wolff–Hardy pain threshold before and at 90 minutes after injection was determined in one group. For this comparison of side-effects, it was found that the conclusions were not valid unless the doses used were equivalent in analgesic power. Then, DL-methadone, L-methadone, and DL-*iso*methadone were as toxic as morphine with respect to symptom production and duration of symptoms; L-*iso*methadone caused less nausea than morphine. All four forms of methadone depressed respiratory rate and slowed the pulse in a manner similar to morphine. Blood pressure was unaffected. It is possible, however, that pain may modify to some extent the incidence and severity of the side-effects which were observed in healthy subjects.

G. B. West

2400. **Observations on the Use of a New Analgesic, NU-2206 (3-Hydroxy-N-Methylmorphinan Hydrobromide)**

L. L. ZAGER, W. W. SAWTELLE, E. G. GROSS, and S. F. NAGFY. *Journal of Laboratory and Clinical Medicine* [*J. Lab, clin. Med.*] **34**, 1530–1537, Nov., 1949. 3 refs.

A new analgesic drug, " NU-2206 " (3-hydroxy-N-methyl-morphinan hydrobromide) was found to have about four times the analgesic potency of morphine when tested on 6 students by the Hardy–Wolff–Goodell method. Nausea and dizziness were produced in all subjects by a dose of 3 mg., together with sedation, inability to concentrate, and gastro-intestinal symptoms: no euphoria was observed. In a clinical trial, doses of 1·5 mg. of NU-2206 were usually ineffective in relieving post-operative pain, and 3 mg. relieved pain in only 3 out of 6 cases. Eleven patients subjected to transurethral resection of the prostate were given 51 doses of 4·5 mg.: all were relieved of pain. Good relief was also afforded to 5 patients with intractable pain due to cancer. No withdrawal symptoms were observed in any of the patients. The results indicate that NU-2206 in doses of 3 to 6 mg. subcutaneously gives analgesia equal to that of morphine (10 to 15 mg.), but with longer action and without the risks of addiction.

John R. Vane

2401. **Some Effects of Dibenzyl-β-Chlorethylamine (Dibenamine) on the Mammalian Heart**

G. H. ACHESON, A. FARAH, and G. N. FRENCH. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 455–465, Dec., 1949. 4 figs., 25 refs.

In the heart and lung preparation from the dog the presence of " dibenamine " at concentrations over 1 in 20,000 caused some failure, shown by rise in auricular pressure, fall in output, and cardiac dilatation; a 1 in 4,000 concentration caused slowing of sinus rate. On the isolated auricle of the rabbit it led to slowing, preceded by a decrease in the maximal rate of stimulation which the auricle could follow for 10 seconds. In doses of 3 to 20 mg. per kg. it decreased the rate of auricular flutter produced by stimulation of the denervated heart of the dog. The protection given by dibenamine against fibrillation due to adrenaline–*cyclo*propane lasts for 1½ to 5 days, but no other cardiac effects of adrenaline are altered.

V. J. Woolley

2402. **Renal Excretion of Digitoxin in Man Following Oral Administration**

M. FRIEDMAN, S. O. BYERS, R. BINE, and C. BLAND. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 468–470, Nov., 1949. 2 refs.

By means of the newly-discovered sensitivity of the embryonic duck heart preparation (Bine and Friedman, *Proc. Soc. exp. Biol., N.Y.*, 1948, **69**, 487) the authors have succeeded in assaying the minute amounts of digitoxin excreted from day to day by normal subjects receiving therapeutic doses. Their 5 subjects each received 1·2 mg. of digitoxin by mouth over a period of 6 hours. During the first day the amount excreted ranged from 44 to 144 μg., during the second from 30 to 68 μg., and during the third from 13 to 46 μg. On the average about 7% of the dose of digitoxin was excreted during the first 24 hours and about 14% during the first 72 hours.

F. N. Fastier

2403. **The Effects of a New Sympatholytic Drug (Priscol) on the Peripheral Circulation in Man**

K. G. WAKIM, G. A. PETERS, and B. T. HORTON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **35**, 50–62, Jan., 1950. 3 figs., 16 refs.

" Priscol " (2-benzyl-4 : 5-imidazoline hydrochloride) has previously been reported to have adrenolytic properties and has been used therapeutically in a variety of peripheral vascular diseases. The authors studied the effect of the intravenous administration of 50 mg. of the drug on the cutaneous and oral temperature and the blood flow in the arms and legs, which was measured by means of the venous occlusion plethysmograph and a compensating spirometer recorder, in 10 human subjects.

The greatest increase in skin temperature was experienced in the legs, particularly in the toes, and in the fingers. The authors presume that as the lowest initial

temperatures were also recorded in these areas, vasoconstriction was present before the injection of priscol, and that the effect of the drug would therefore be less marked in regions where vasodilatation was present initially. This temperature rise persisted in all cases for more than an hour, and in a few cases in which skin temperatures were recorded again about 5 hours after administration of the drug they were still found to be higher than in the control. The oral temperature was slightly reduced during the first half-hour after administration of the drug, which the authors attribute to the facilitated elimination of body heat through the cutaneous vasodilatation produced by the drug, but was normal again within one hour. The rise of skin temperature coincided with an increase of blood flow in both arms and legs. The combined average increase in both arms was 89% after 5 minutes, and was still 46% after 45 minutes.

The pulse volume was increased in the majority of subjects, and there was also a transient increase in the heart rate over a period of 2 minutes from the time of injection, the increase ranging from 6 to 48 beats per minute (average 26). On the whole, within 15 minutes the heart rate had returned to its pre-injection value. The changes in blood pressure were moderate, but statistically significant. There was an average increase of 6 mm. Hg in the systolic pressure, and an average decrease of 11 mm. Hg in the diastolic value. Within 15 minutes the blood pressure had returned to the pre-injection level.

Compared with the authors' previous observations on the effects of intravenous administration of histamine (*J. Lab. clin. Med.*, 1949, **34**, 380), the effect of priscol on the peripheral circulation was less marked initially, but considerably more prolonged.

H. Lehmann

2404. **Assay in Man of the Chemical Fractions of *Veratrum viride*, and Identification of the Pure Alkaloids Germitrine and Germidine as Potent Hypotensive Principles Derived from the Drug**

E. D. Freis, J. R. Stanton, and F. C. Moister. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **98**, 166–173, Feb., 1950. 2 figs., 8 refs.

The crude powdered root and rhizome of *Veratrum viride* have become of interest to clinicians recently because of their power to lower blood pressure in essential hypertension. This effect is, however, inconstant and often accompanied by toxic effects. Various alkaloids and fractions have recently been isolated from the preparations, and the present investigation had as its objects the identification of the hypotensive principle or principles, their separation from the toxic principle if possible, and the isolation of pure crystalline compounds for clinical use.

Fractions and pure alkaloids were tested by oral administration to patients with hypertension in the wards of the Massachusetts Memorial Hospital and the Veterans Administration Hospital, Washington. Over 400 assays were carried out on 102 fractions. Pure active alkaloids were given intravenously dissolved in acetic acid and diluted in saline.

The cardiovascular effects were found to be largely due to two hitherto undescribed crystalline ester alkaloids, germitrine and germidine. The effective dose of the former by mouth is 1 to 1·2 mg., and intravenously 0·05 to 0·06 mg. Such doses lowered systolic and diastolic blood pressure by significant amounts. The effective dose of germidine was 2·5 to 3·5 mg. by mouth and 0·1 to 0·38 mg. intravenously. A third crystalline alkaloid, germerine, has similar properties but probably does not occur as such in the root, being derived by partial hydrolysis from germitrine. The activity of germerine is of the same order as that of germidine. Complete hydrolysis of all these three ester alkaloids to germine results in loss of hypotensive action.

Unfortunately toxic effects, such as nausea, vomiting, salivation, and substernal tingling, were as prone to occur after administration of the alkaloids as of the crude extract of *Veratrum viride*.

S. S. B. Gilder

2405. **Studies on the Mode of Action of Ergotamine, Dihydroergotamine, and Dihydroergocornine in Normal Subjects.** (Untersuchungen über das Wirkungsbild der Mutterkornalkaloide Ergotamin, Dihydroergotamin und Dihydroergocornin am gesunden Menschen)

H. Gatzek, K. Matthes, and K. Mechelke. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **207**, 720–730, 1949. 4 figs., 21 refs.

The action of the ergotamine alkaloids " gynergen " (ergotamine tartrate), " DHE 45 " (dihydroergotamine), and " DHO 180 " (dihydroergocornine) was investigated in normal subjects by the methods of Matthes (*Dtsch. med. Wschr.*, 1947) for continuous recording of pulse rate, systolic blood pressure, respiration, oxygen saturation, and volume and temperature of ear and finger. The results were compared with those obtained when the drugs were administered after small doses of adrenaline.

Ergotamine tartrate, 0·25 mg. intravenously, caused a slight but prolonged rise in blood pressure. After an initial rise in pulse rate accompanied by deeper and more rapid respiration, the pulse rate fell when the blood pressure rose. After 10 minutes the pulse rate returned to its normal value. After a transient rise in ear volume there was prolonged vasoconstriction without appreciable change in oxygen saturation, owing to the action of the alkaloid on the smooth muscle of the vessels. This was most marked in the ear, but could be demonstrated in the hand with larger doses. With smaller doses the volume, oxygen saturation, and temperature of the hand may increase.

Dihydroergotamine, 1 mg. intravenously, also produced definite decrease in the ear volume with unchanged oxygen saturation and an accompanying fall in temperature. The volume of the finger increased with increase of oxygen saturation and a corresponding rise in temperature. Blood pressure showed a slight prolonged rise (10 to 15 mm. Hg), respiration rate fell slightly, and respiration became more shallow. There was no change in pulse rate.

Dihydroergocornine, 0·5 mg. intravenously, produced a fall in blood pressure (20 mm. Hg). There was

simultaneous vasodilatation in the ear with increase in temperature and unchanged oxygen saturation. In the finger the vasodilatation was accompanied by an increase in oxygen saturation and a rise in temperature. Pulse rate fell slightly and respiration was unchanged.

The sympatholytic action of these drugs could not be demonstrated. A reduction or abolition of the adrenaline effect could never be shown. On the contrary the alkaloids enhanced the action of adrenaline on the circulation. *Vera N. Warren*

2406. **The Renal Hemodynamic Effects of Dihydroergocornine (DHO-180) in Man**
A. P. Crosley, A. J. Cummins, H. G. Barker, and J. K. Clark. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **98**, 138–143, Feb., 1950. 1 fig., 18 refs.

Dihydroergocornine (" DH-180 ") is an adrenergic blocking agent and also reduces the excessive cerebral vascular resistance in hypertension.

The present authors studied its effects on renal haemodynamics in 5 normal subjects and 5 patients with hypertension. The drug was injected intramuscularly in a dose of 0·5 mg., and glomerular filtration rate (endogenous creatinine clearance), effective renal plasma flow (*p*-aminohippurate clearance), blood pressure, and pulse rate were measured both before and after the injection.

A statistically significant fall in blood pressure occurred after 20 to 40 minutes in all but one person, the fall being earlier and more profound in cases of hypertension. Pulse rate was unchanged. Effective renal plasma flow decreased somewhat more than glomerular filtration rate, the filtration fraction and renal peripheral resistance increasing for periods up to 2½ hours. The only side-effect, observed in 9 subjects, was nasal stuffiness.

It would appear that the adrenergic blocking effect of the drug which would cause renal vasodilatation is overcome by a protective mechanism, whereby blood is diverted from the kidney to the brain.
S. S. B. Gilder

2407. **The Effect of Intramuscular Dihydroergocornine on the Cerebral Circulation in Normotensive Patients**
J. H. Hafkenschiel, C. W. Crumpton, and J. H. Moyer. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **98**, 144–146, Feb., 1950. 11 refs.

The effects of intramuscular injection of dihydroergocornine on cerebral blood flow and cerebral oxygen consumption were studied in 5 subjects without organic disease and with normal blood pressure. The dose was 0·4 mg., cerebral blood flow being measured by the nitrous-oxide technique before the injection and when the blood pressure was at its lowest level, usually 60 to 70 minutes after the injection. In some instances samples of blood were taken simultaneously from an artery and the internal jugular vein and analysed for oxygen and carbon-dioxide content.

Mean cerebral blood flow, cerebral oxygen uptake, and cerebral vascular resistance (mean arterial blood pressure divided by cerebral blood flow in ml. per 100 g. brain per minute) decreased only slightly (insignificantly) after the injection, although there was a significant fall in mean arterial blood pressure averaging 17%. Arterio-venous oxygen difference and jugular oxygen content were little changed when the circulation became stabilized at a lower level of blood pressure. This behaviour of vascular resistance was in sharp contrast to the decrease previously observed in cases of hypertension.
S. S. B. Gilder

2408. **Effect of Cocaine and Ephedrine on the Vasoconstriction Produced by Acute Oxygen Lack.** [In English]
D. F. Marsh and E. J. van Liere. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **81**, 207–210, 1950. 1 fig., 11 refs.

In anaesthetized dogs, the pressor response which occurs when the animal breathes air of low oxygen content is much increased after the injection of cocaine. A similar but smaller increase in response occurs after ephedrine administration. *Derek R. Wood*

2409. **Cardio-Respiratory Effects Following Intravenous Administration of Some Antihistaminic Drugs**
O. Orias, J. L. Gilbert, and C. McC. Brooks. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 492–498, Dec., 1949. 6 figs., 8 refs.

" Antistin ", " benadryl ", " pyribenzamine ", " thenylene ", and " thephorin " were given intravenously in doses of 1, 4, or 8 mg. per kg. to anaesthetized cats. The smallest dose had very little effect; usually there was a slight fall in blood pressure. The larger doses caused a severe fall in blood pressure and transient apnoea, with changes in the electrocardiogram consisting of a prolongation of the P–R interval and the QRS complex. The most powerful drug was thephorin, followed by thenylene, antistin, pyribenzamine, and benadryl in decreasing order. Doses larger than 8 mg. per kg. caused severe fall in blood pressure, various arrhythmias, and, ultimately, either respiratory or cardiac failure.
V. J. Woolley

2410. **Liberation of Histamine by Adrenaline from Isolated Lung.** [In English]
J. Koch and J. Szerb. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **81**, 91–98, 1950. 1 fig., 35 refs.

The amount of histamine liberated from the isolated rat lung perfused with Ringer's solution is increased by the addition of 0·5 mg. of adrenaline per 100 ml. of perfusing fluid, the amount of histamine liberated being from 25 to 80% of that presumed to be present in the lung. The adrenolytic substance, dihydroergocornine, does not prevent this effect. It is considered that the liberation of histamine is due to an oxidation process by which protein-bound histamine is released, because it could be prevented by addition to the perfusing fluid of sodium cyanide (0·001 M). The possibility is suggested that the liberation of histamine plays a part in the development of pulmonary oedema after the intravenous injection of adrenaline. *Derek R. Wood*

2411. **On the Actions of Noradrenaline, Adrenaline and *Iso*propyl Noradrenaline on the Arterial Blood Pressure, Heart Rate and Muscle Blood Flow in Man**
H. BARCROFT and H. KONZETT. *Journal of Physiology* [*J. Physiol.*] **110**, 194–204, 1949. 4 figs., 24 refs.

A study was made of the effects of noradrenaline, adrenaline, and N-*iso*propylnoradrenaline, given by intra-arterial or intravenous infusion to normal subjects, on blood flow in the forearm and calf (measured by the plethysmographic method), arterial blood pressure, and heart rate. Noradrenaline caused constriction of cutaneous and muscle vessels, bradycardia, and a rise in both systolic and diastolic pressures. Adrenaline caused a transient vasodilatation, a rise in systolic pressure and no change, or a slight fall, in diastolic pressure, and a tachycardia which subsided to some extent before the end of the infusion period (3 minutes). *Iso*propylnoradrenaline caused cutaneous dilatation, transient muscle dilatation, persistent tachycardia, rise in systolic pressure, and a marked fall in diastolic pressure. No symptoms were observed with noradrenaline. Adrenaline often caused hyperventilation and palpitation, with facial pallor during the infusion and flushing afterwards. The same symptoms were observed with the *iso*propyl derivative except that palpitation was more marked and persistent. *R. A. Gregory*

2412. **Microscopic Studies on Vascular Reactions to Ergonovine Maleate in the Living Animal**
R. G. ABELL. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 466–474, Dec., 1949. 11 figs., 14 refs.

Newly-formed arterioles, venules, and capillaries were examined and photographed at magnifications of 200 and 400 diameters in a transparent chamber implanted in a rabbit's ear. Injections of 0·005 to 4 mg. of ergometrine maleate caused a transient vasoconstriction proportional to dose. Injections given once daily caused identical responses. Injections at 15- to 30-minute intervals resulted in progressively less constriction and finally dilatation. Large doses produced no change in the response to adrenaline. Moderate doses caused no changes in the endothelium. After very large doses there was a transient adhesion of leucocytes to the vessel walls. *V. J. Woolley*

2413. **On the Pharmacology of Iodomethylate of Dimethylamino-1-methylene-dioxy-2,3-propane (2249 F—Dilvasène).** [In English]
R. VERBEKE and G. R. DE VLEESCHHOUWER. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **81**, 1–16, 1950. 12 figs., 14 refs.

The iodomethylate of dimethylamino-1-methylene-dioxy-2 : 3-propane (" dilvasene "), a compound with little muscarinic, but considerable nicotinic, action has been used clinically in peripheral vascular and other diseases. This detailed report of its pharmacology in the anaesthetized dog comes from the J. F. Heymans Institute of Pharmacology, University of Ghent. Doses of 0·001 to 0·05 mg. of dilvasene per kg. body weight intravenously caused a short-lived fall of blood pressure, with salivation and respiratory stimulation. Larger doses caused temporary arrest of the heart, followed by a prolonged bradycardia. Other effects included contraction of the smooth muscle of the bladder, the bronchioles, and the intestine. Still larger doses (1 mg. per kg.) were followed by muscular fasciculation, convulsions, and apnoea, the animal dying of cardiac and respiratory failure. The effects on the heart are due to the action of the drug on vagal synapses. Atropine, " parpanit " and " diparcol " opposed the bradycardia caused by moderate doses of dilvasene. Small doses caused vasodilatation when injected into the femoral artery whether the limb was denervated or not, thus explaining the fall in blood pressure observed with such doses. After administration of atropine, large doses of dilvasene caused a rise in blood pressure owing to stimulation of the sympathetic synapses and the adrenal medulla; however, when tetraethylammonium was injected after atropine, dilvasene caused a fall in blood pressure. Respiration was stimulated reflexly via the carotid body chemoreceptors, but large doses of the drug caused apnoea by its action on the respiratory centre. This was not opposed by atropine, parpanit, or diparcol. These substances did, however, antagonize the action of dilvasene on salivary secretion, intestine, and bladder, but did not affect the muscular fasciculation and convulsions caused by larger doses. It is concluded that dilvasene is primarily a nicotinic compound and that it has no muscarinic action. [This conclusion appears to be only relatively true in view of the hypersalivation, increased peristaltic activity, and contraction of the bladder which the drug causes and which atropine suppresses.] *Derek R. Wood*

2414. **A Neuropharmacological Study on the Effect of " Myanesin " (" Tolserol ") on Motor Systems**
E. HENNEMAN, A. KAPLAN, and K. UNNA. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 331–341, Nov., 1949. 7 figs., 15 refs.

The knee-jerk of cats lightly anaesthetized with pentobarbitone was facilitated when lateral reticular nuclei (4 to 5 mm. from the midline) in the region extending from the hypothalamus to the lower pons were stimulated. An intravenous dose of 25 mg. of " myanesin " per kg. prevented this facilitation without affecting the knee-jerk itself. The effect of the myanesin lasted for from 250 to 300 minutes, but in non-anaesthetized decerebrate cats the action was briefer, lasting only for 30 to 40 minutes.

Stimulation of medial reticular nuclei (within 2 mm. of the midline) in the medulla inhibited the knee-jerk. The inhibition was reduced by a dose of 25 mg. of myanesin per kg. but was not completely abolished by three to four times this amount.

Inhibition of the knee-jerk produced by stimulation of the cerebral cortex, the caudate nucleus, or the anterior lobe of the cerebellum was reduced by 12 mg. of myanesin per kg., and abolished by 25 mg. per kg.

In the " spinal " cat, stimulation of the sciatic nerve caused " crossed extension " of the contralateral leg, abolished by 25 mg. of myanesin per kg. Inhibition of

the knee-jerk due to stimulation of the nerve to the contralateral quadriceps muscle was prevented by giving myanesin, but the drug did not even reduce the inhibition elicited by stimulating the ipsilateral sciatic nerve. Some of the non-anaesthetized " spinal " animals had grossly irregular knee-jerks which were " regularized " by a dose of 2 mg. of myanesin per kg.

The importance of the results in relation to the site of action of myanesin and to its use in the treatment of spasticity are discussed. *P. A. Nasmyth*

2415. **The Effect of α, β-Dihydroxy-γ-(2 Methylphenoxy) Propane (" Myanesin ", " Tolserol ") on Experimental Spasticity in Cats**

E. HENNEMAN and J. SCHERRER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 342–348, Nov., 1949. 5 figs., 5 refs.

In decerebrate cats the knee-jerk elicited once a second was full but irregular and followed by clonus. After 15 mg. " myanesin " per kg. had been given intravenously it became regular and reduced in amplitude, and the clonus disappeared. The effect passed off in 30 to 40 minutes.

Removal of the anterior lobe of the cerebellum from decerebrate cats increased the tone in both extensors and flexors. In consequence, the knee-jerk was reduced in amplitude and there was no clonus. Myanesin, 10 mg. per kg., in these animals increased the amplitude and promoted the development of clonus. A second dose, 5 minutes later, reduced the amplitude and the clonus. After a further 5 minutes a third dose relieved the remaining spasticity and eliminated the clonus.

In chronic experiments, spasticity was produced by inflicting surgical lesions in various suppressor regions, all having connexions with bulbar reticular inhibitory centres. All these spastic cats had well-marked stretch reflexes and, without exception, they responded well to 25 mg. of myanesin per kg. by showing a great reduction in muscle potentials during stretch.

It is claimed that the experiments indicate that discrepancies in the results of clinical trials with myanesin are not due to the variety of the lesions causing spasticity. *P. A. Nasmyth*

2416. **Effects of Folic Acid on Respiratory and Nitrogen Metabolism**

R. C. GRUBBS, J. TROSSBACH, B. C. HOUGHTON, and F. A. HITCHCOCK. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 327–342, Dec., 1949. 3 figs., 32 refs.

Metabolic effects of folic acid were studied at Ohio State University on 7 normal subjects and 6 male hospital patients (3 with pernicious anaemia, 1 with Hodgkin's disease, 1 with hepatic cirrhosis and 1 with idiopathic steatorrhoea). Studies lasted for 4 to 6 weeks and, during part of this time, 30 mg. folic acid was given intramuscularly daily. Urine and faeces were analysed for nitrogen, and the nitrogen intake was also calculated. Studies of respiratory metabolism at rest and, when possible, during mild exercise were carried out, and blood counts were made five times a week. Two additional patients received liver extract instead of folic acid, and one patient given folic acid subsequently received liver extract for comparison.

Clinically, folic-acid administration caused euphoria, increase in appetite, and increase in calorie intake in all 6 patients. In normal subjects erythrocyte and reticulocyte counts remained unchanged but in the 3 patients with pernicious anaemia the expected rise in both counts occurred. There was no significant change in basal oxygen consumption in normal subjects, but in all 6 patients there was a fall, statistically significant in 3 and correlated with the changes in the peripheral blood. Basal oxygen consumption also decreased definitely in 2 out of 3 patients receiving liver. In normal subjects there was no change in carbon-dioxide production, but the latter decreased in all but one of the patients. Basal nitrogen excretion underwent no change. Basal non-protein respiratory quotient rose in all but two normal subjects and in 3 patients. There was no significant change in the percentage of total basal calories obtained from protein in any subject, but in 5 out of 7 normal subjects and 3 patients the percentage derived from carbohydrates rose.

Specific dynamic action rose in 5 out of 7 normal subjects and in 5 patients. Faecal nitrogen increased and nitrogen retention decreased in normal subjects, but retention increased in all patients. This retention was due to increased protein intake, decrease in faecal excretion of nitrogen, and decrease in urinary excretion of nitrogen (in 3 out of 5 cases).

It would appear that in patients folic acid increased nitrogen absorption from the gastro-intestinal tract and decreased de-amination of amino-acids by the liver, an increased proportion of the latter being used to synthesize haemoglobin and tissue proteins. *S. S. B. Gilder*

2417. **The Effects of 4-Hydroxycoumarin Anticoagulant No. 63 Upon the Prothrombin Time in Dogs and Human Beings**

W. D. BATTLE, R. T. CAPPS, O. S. ORTH, and O. O. MEYER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **35**, 8–15, Jan., 1950. 4 figs., 8 refs.

The authors have investigated the effects of the dicoumarol derivative known as 4-hydroxycoumarin anticoagulant No. 63 (Ikawa *et al.*, *J. Amer. chem. Soc.*, 1944, **66**, 902). Unlike dicoumarol this compound did not produce toxic lesions of small blood vessels even when given to dogs in lethal doses (5 mg. per kg. body weight daily for 6 to 30 days). The gross pathological findings in the 6 animals given this dosage included bilateral haemorrhagic pleural effusion and subcutaneous haemorrhages in 3 cases, and haemopericardium in one; in one pregnant animal there was massive uterine haemorrhage, and in another, death of the foetus and later of the mother occurred, with haemorrhage of the Fallopian tubes and ureters. Microscopical findings consisted of oedema of the lungs in 3 dogs and extensive haemorrhage of the lungs in one other. No dog died as the result of a single dose of even as much as 100 mg. per kg.

The powdered drug was then given in gelatin capsules to 15 human subjects, most of whom received single

doses, while in 6 cases repeated doses were given. An initial dose of 2 mg. per kg. was found in most instances to raise the prothrombin time to the desired therapeutic level within 24 to 48 hours. The prothrombin time returned to its original level after a single dose in an average of 8·75 days, with extremes of 4 and 14 days. In 5 of the 6 trials with repeated doses an initial dose of 2 mg. per kg. was given, and it was not difficult to maintain the prothrombin time at the desired level by administering 0·5 to 1 mg. per kg. at intervals of 1 to 14 days. The sixth patient was given only 1 mg. per kg. initially, his prothrombin time being initially higher than the average.

There were no changes in the blood count, urinary findings, or results of hepatic function tests (including cephalin-cholestrol and thymol-turbidity tests, icterus index, and serum bilirubin, urinary urobilinogen, and serum protein determinations) in any of the patients studied. It seems established that the potency of 4-hydroxycoumarin anticoagulant No. 63 is 2 to 3 times that of dicoumarol, but the authors themselves point out that this in itself cannot be construed as advantageous.

H. Lehmann

2418. **Clinical Tests of a New Coumarin Substance. A Report to the Medical Research Council**
C. C. BURT, H. P. WRIGHT, and M. KUBIK. *British Medical Journal* [*Brit. med. J.*] **2**, 1250–1254, Dec. 3, 1949. 7 figs., 7 refs.

The treatment of 126 subjects, including cases of post-operative thrombosis, pulmonary embolism, and spontaneous venous, puerperal, and arterial thrombosis, with a new coumarin product, bis-3 : 3′-(4-oxycoumarinyl)-ethyl acetate (B.O.E.A.) is reported. A dose of 0·9 to 1·2 g. was given on the first 2 days, and 0·3 to 0·6 g. was usually adequate thereafter, the dosage being regulated according to the blood prothrombin level, which was checked daily. To patients needing immediate therapy, heparin was given for the first 24 to 48 hours. The blood prothrombin level was reduced to under 50% of normal within 36 hours in 100 of the 126 patients, and returned to over 50% of normal within the same time after cessation of treatment. Compared with a small group of patients treated with dicoumarol, the response to B.O.E.A. was more rapid. No toxic effects were observed, except for slight nausea and vomiting in a few subjects.

John R. Vane

2419. **Cardiopressive Effects of Thiomerin: Cardioprotective Attempts with BAL, Ascorbic Acid and Thiamin**
A. RUSKIN and J. E. JOHNSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 572–576, Dec., 1949. 4 figs., 9 refs.

2420. **Cardiopressive Effects of Mercurial Diuretics. Cardioprotective Value of BAL, Ascorbic Acid and Thiamin**
A. RUSKIN and J. E. JOHNSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 577–583, Dec., 1949. 6 figs., 13 refs.

CHEMOTHERAPY

2421. **The Effect of Folic-acid Derivatives on Sarcoma**
E. B. SCHOENBACH, A. GOLDIN, B. GOLDBERG, and L. G. ORTEGA. *Cancer* [*Cancer*] **2**, 57–64, Jan., 1949. 4 figs., 28 refs.

Aminopterin (N-{4-[(2 : 4-diamino-6-pteridyl)-methyl amino] benzoyl} glutamic acid) inhibited growth of "sarcoma 180" in male CF1 mice, when given in daily doses of 0·2 to 0·3 mg. per kg. (10 ml. per kg. in 0·9% saline) by the intravenous, intraperitoneal, or subcutaneous route. The mice lost weight, but the reduction in tumour weight compared with that in controls was much greater than that caused by a similar loss in body weight through underfeeding. Histological examination of tumours showed a decrease in number and size of necrotic areas which normally develop in this sarcoma, and there was no vascular damage or haemorrhage. In blood from the tail vein of mice that had received a single injection of 25 mg. aminopterin per kg. there was a slight leucopenia. Teropterin and diopterin in daily doses of 500 mg. per kg. had no effect.

E. Boyland

2422. **Cancer Chemotherapy. Analysis of Results of Different Screening Techniques with Nitrogen-mustard Analogues**
D. M. SHAPIRO, A. GOLDIN, B. H. LANDING, A. D. BERGNER, F. FAIMAN, and B. GOLDBERG. *Cancer* [*Cancer*] **2**, 100–112, Jan., 1949. 14 refs.

The chemotherapeutic effect of 36 analogues of nitrogen mustard was studied on "sarcoma 180", the following five methods being used. (1) Repeated doses (at maximum tolerated cumulative dose) and haematoxylin-eosin sections. (2) Repeated doses (at maximum tolerated cumulative dose) and aceto-orcein smears. (3) Single large doses (2 LD 50) and haematoxylin-eosin sections. (4) Single large doses (2 LD 50) and aceto-orcein smears. (5) Repeated doses (at maximum tolerated cumulative dose) and inhibition of tumour weight. If results by all methods were considered, none of the compounds was more effective than methyl-bis (β-chloroethyl)amine and tris (β-chloroethyl) amine (both known to be effective in human cancer). The tumour weight method did indicate that certain mustards were more effective, and with nine of these compounds the body-weight loss was probably not enough to cause inhibition of tumour growth. Statistical analysis showed that there was no correlation between the results of these five methods which could not be due to chance.

E. Boyland

2423. **Systemic Pathological Effects of Nitrogen Mustards, and a Comparison of Toxicity, Chemical Structure, and Cytotoxic Effect, with Reference to the Chemotherapy of Tumors**
B. H. LANDING, A. GOLDIN, H. A. NOE, B. GOLDBERG, and D. SHAPIRO. *Cancer* [*Cancer*] **2**, 1055–1066, Nov., 1949. 1 fig., 13 refs.

The relation of chemical structure to toxicity and pathological effects on mice was studied in the case of

34 nitrogen mustards and 6 chemically related compounds. Nitrogen mustards with two or more (2-chloroethyl) side chains and with medium lethal doses from 10 to 1,000 micromoles per kg. are most toxic to rapidly proliferating cells and may therefore be most useful in chemotherapy of human tumours.

E. Boyland

2424. **The Effects of a Nitrogen Mustard [Tris(-Chloroethyl)amine] on Regenerating Rat Liver**
B. H. LANDING, J. C. SEED, and W. G. BANFIELD. *Cancer* [*Cancer*] **2**, 1067–1074, Nov., 1949. 4 figs., 10 refs.

Nitrogen mustard was injected intravenously into partially hepatectomized rats and caused some slowing of mitosis, but the cytotoxic effects were small. The relative immunity of liver cells to toxic effects of nitrogen mustard is therefore not due to the low rate of mitosis.

E. Boyland

2425. **Testicular Lesions in Mice Following Parenteral Administration of Nitrogen Mustards**
B. H. LANDING, A. GOLDIN, and H. A. NOE. *Cancer* [*Cancer*] **2**, 1075–1082, Nov., 1949. 8 figs., 17 refs.

Intraperitoneal injection of nine nitrogen mustards caused testicular lesions in young adult mice. The degenerative changes were similar to those produced by *x* rays or malnutrition. Recovery of spermatogenic function occurred 4 weeks after exposure.

E. Boyland

2426. **Nitrogen Mustards. Statistical Analysis of Effects on Sarcoma 180 and Viscera of Normal Mice in Relation to Toxicity and Structure**
B. H. LANDING and F. F. EISENBERG. *Cancer* [*Cancer*] **2**, 1083–1086, Nov., 1949. 1 fig., 4 refs.

Data on the toxicity, structure, effects on tissue, and effects on mouse sarcoma 180 of a series of nitrogen mustards are analysed statistically. There is no evidence that this tumour is more susceptible than normal susceptible tissues. Five methods of evaluating tumour susceptibility show insignificant correlation with each other; hence the results obtained with one screening technique cannot be compared directly with those obtained by a different technique. *E. Boyland*

ANTIBIOTICS

2427. **A Clinical Study of the Toxic Effects of Dihydrostreptomycin and Streptomycin**
C. M. DOMON, P. C. KILBOURNE, and E. Q. KING. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **60**, 564–575, Nov., 1949. 1 fig., 6 refs.

To obtain information on the relative toxicity of streptomycin and dihydrostreptomycin a series of 20 patients suffering from pulmonary tuberculosis was divided into two comparable groups of 10 patients and each treated with one of the two drugs for up to 3 months. As the series was so small it was necessary to employ a dose high enough to produce significant toxic manifestations with at least one of the drugs. The daily dose of 3 g., in 8-hourly doses of 1 g., was chosen. Treatment was stopped at the first definite indication of any toxic effect, unless there was definite justification for continuing. The main indications for the discontinuation of treatment were: vestibular dysfunction, manifested by ataxia, nausea, and vomiting, visual disturbance, dizziness, tinnitus, spontaneous nystagmus, deafness increasing during treatment, blood dyscrasias, and exfoliative dermatitis. In addition pain and local reaction at the site of injection, as well as drug fever, were watched for and recorded.

All patients were questioned daily and examined for toxic symptoms, care being taken not to ask leading questions. Before administration of either drug, complete clinical, radiological, and laboratory examinations were carried out, including the construction of an audiogram and a caloric stimulation test (modified Glorig and Fowler method), and were repeated at regular intervals thereafter.

All patients had a normal caloric response and audiogram before treatment, although a number had been treated with streptomycin previously; none had received streptomycin for the 6 months preceding the trial. Of those given streptomycin sulphate 8 patients developed vestibular damage necessitating discontinuation of treatment between the 18th and 66th days. Symptoms developed in most patients during the 3rd week of treatment. Previous streptomycin treatment had apparently no bearing on the result. In one patient caloric response became absent 3 weeks after completion of treatment. None of the patients given dihydrostreptomycin showed any vestibular disturbance during the whole course. The difference between the two groups, in spite of the small numbers, is statistically significant. No damage to the hearing apparatus was observed in either group.

Previous studies on the toxicity of dihydrostreptomycin, in which the hydrochloride was used, gave results markedly different from those above. In the present investigation the hydrochloride was used for 6 weeks only and the course completed with the sulphate. Further study is needed to assess clearly the relative toxicity of the two salts of dihydrostreptomycin.

E. Nassau

For treatment of tuberculosis with streptomycin see Section Infectious Diseases, pp. 663–6.

2428. **Effect of Aureomycin on the Herpes Simplex Virus in Embryonated Eggs**
G. D. BALDRIDGE and H. BLANK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 560–563, Dec., 1949. 1 fig., 7 refs.

The toxicity of aureomycin for 10- to 12-day-old chick embryos was first determined. The eggs were prepared by the false-sac technique, and the dose of aureomycin, dissolved in 0·2 ml. of gelatin saline, was inoculated into the " dropped " chorio-allantois. The eggs were incubated at 96° F. (35·6° C.) and 76% relative humidity and

were candled twice daily, death of the embryo being taken as the end point. Two batches of aureomycin were used. With batch A the LD 50 was 20 mg. per kg. body weight. The other batch was considerably more toxic. Under the same conditions, both aureomycin inactivated by heating at 56° C. for 5 days and penicillin were found to be non-toxic.

The virus used had been adapted from the HF Rockefeller strain by 129 serial passages on the chorio-allantoic membrane, and when properly diluted killed 95 to 100% of chick embryos between the 69th and 90th hours. The effect of aureomycin on the virus *in vitro* was studied by incubating the drug with a 10% suspension of infected membrane at room temperature for 4 hours, and then injecting it on to the chorio-allantoic membrane, the mixture being diluted enough to eliminate any effect of the drug *in vivo*. Under these conditions aureomycin had no appreciable effect on the virus. To determine the effect of aureomycin on the virus *in vivo* the drug was first injected into the yolk sac, which was inoculated with the virus 30 minutes later. Additional experiments were carried out on the chorio-allantoic membrane, the same technique being used as for the toxicity studies. In one of these the virus was injected before, and in the rest 30 minutes after, the antibiotic, while in several experiments a series of 3 or 6 doses of aureomycin were given at 12-hour intervals. There was no significant difference in mortality or period of survival between embryos treated with either batch of aureomycin and the controls.

It is thus concluded that aureomycin is more toxic for the chick embryo than for most other laboratory animals, and that it has no action on the herpes simplex virus comparable to its effect on the larger viruses.

Mary Barber

See also Section Genito-Urinary Disorders, Abstracts 2707–8.

2429. **Search for Antibiotics Active Against *Mycobacterium tuberculosis*. 1. A Streptothricin-like Antibiotic from a *Streptomyces* sp.**

R. S. Weiser, G. M. Gardner, J. S. Lefler, and L. St. Vincent. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 283–287, Nov., 1949. 14 refs.

2430. **Diplomycin (Diplomycin)**

B. Viking. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **111**, 1443–1450, Dec. 22, 1949. 2 figs., 4 refs.

This is a preliminary report on trials of " diplomycin " which were conducted at the University Surgical Clinic of Aarhus Municipal Hospital from July, 1949, onwards. Diplomycin is an antibiotic extracted from a diplococcus isolated by Noster in 1945. It is bactericidal to a number of Gram-positive and Gram-negative organisms as well as to *Mycobacterium tuberculosis*. *In vitro* tests reported in this paper showed that its action upon staphylococci, pneumococci, and coliform bacilli was comparable to or exceeded that of penicillin and that of streptomycin.

During the five months under review 150 patients were treated, 75 with an ointment, 13 with an emulsion applied to the nasopharynx, 14 with vaginal suppositories, and 48 with intravenous injections. The effects noted included rapid healing of ulcers and bedsores, cessation of vaginal discharge (frequently associated with a *Trichomonas* infection), rapid improvement in cases of sinusitis and pharyngitis, and finally a rapid response to parenteral therapy in such diverse conditions as infective mastitis, lymphadenitis, osteomyelitis, non-specific epididymitis, and *Proteus* pyelitis which had proved resistant to penicillin, streptomycin, and sulphonamides. Favourable results were also observed in a case of bilateral renal tuberculosis and in a case of tuberculous adenitis with fistulae.

B. Nordin

2431. **Terramycin, a New Antibiotic**

A. C. Finlay, G. L. Hobby, S. Y. P'An, P. P. Regna, J. B. Routien, D. B. Seeley, G. M. Shull, B. A. Sobin, I. A. Solomons, J. W. Vinson, and J. H. Kane. *Science* [*Science*] **111**, 85, Jan. 27, 1950.

" Terramycin " is the name given to a crystalline antibiotic obtained by the authors from broth cultures of a new actinomycete, *Streptomyces rimosus*, isolated from soil. Various physico-chemical properties of the new antibiotic are described. It is water-soluble and has a low degree of toxicity for animals. It is highly active against a large number of micro-organisms, both Gram-negative and Gram-positive, *in vitro*, and has been found effective *in vivo* against infections in mice due to *Streptococcus haemolyticus*, *Diplococcus pneumoniae*, *Klebsiella pneumoniae*, and *Salmonella typhi*.

A. Brown

For antibiotics in treatment of infectious diseases see pp. 657–71.

2432. **Ayfivin: An Antibiotic from *B. licheniformis*: Production in Potato-dextrose Medium**

A. Arriagada, M. C. Savage, E. P. Abraham, N. G. Heatley, and A. E. Sharp. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **30**, 425–427, Oct., 1949.

2433. **Ayfivin: Production in Chemically Defined Media and Comparison with Licheniformin**

G. M. Hills, F. C. Belton, and E. D. Blatchley. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **30**, 427–443, Oct., 1949. 4 figs., 22 refs.

2434. **Ayfivin: Extraction, Purification, and Chemical Properties**

V. E Sharp, A. Arriagada, G. G. F. Newton, and E. P. Abraham. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **30**, 444–457, Oct., 1949. 6 figs., 17 refs.

2435. **Prodigiosin. I. Antibiotic Action on *Coccidioides immitis in vitro***

A. Lack. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 656–658, Dec., 1949. 12 refs.

2436. **The Isolation of Antibiotics Produced by *Proactinomyces* (*Nocardia*) *gardneri***
R. Q. MARSTON. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **30**, 398–407, Oct., 1949. 7 figs., 11 refs.

2437. **The Antibacterial and Pharmacological Properties of the Proactinomycins A, B and C**
R. Q. MARSTON and H. W. FLOREY. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **30**, 407–418, Oct., 1949. 9 figs., 9 refs.

PENICILLIN

2438. **Comparison of Oral Penicillins**
W. P. BOGER, J. O. BEATTY, and H. F. FLIPPIN. *Transactions and Studies of the College of Physicians of Philadelphia* [*Trans. Stud. Coll. Phys. Phila.*] **17**, 105–114, Dec., 1949. 5 figs., 29 refs.

To each of 6 subjects 5 different preparations of penicillin were given orally and sodium penicillin intramuscularly in single doses of 200,000 units and the plasma penicillin concentration over the next 3½ hours estimated and compared. The preparations given by mouth consisted of sodium, potassium, and aluminium salts of penicillin, and procaine penicillin (2 differently buffered potassium penicillin preparations being included). Widely differing results were obtained. The aluminium penicillin preparation with a sodium benzoate buffer gave significantly higher plasma concentrations than any of the other oral preparations. With this preparation the ratio of the plasma penicillin concentration after intramuscular to that after oral administration was 14 to 1 half an hour after administration, 3 to 1 at 1½ hours, and 1 to 1 at 2½ and 3½ hours. With the other preparations the half-hour figures were as high as 35 to 1, and did not fall below 3 to 1 at 3½ hours. Over a 3½-hour period, one-sixth as much penicillin was recovered from the urine after oral as after intramuscular administration. The authors point out that although this series is a small one the conditions were rigidly controlled, and their figures have been subjected to statistical analysis and found to be highly significant.
A. W. H. Foxell

2439. **The Use of Procaine Penicillin with Aluminium Monostearate in Adults**
E. J. WAYNE, J. COLQUHOUN, and J. BURKE. *British Medical Journal* [*Brit. med. J.*] **2**, 1319–1322, Dec. 10, 1949. 18 refs.

The concentration of penicillin in the serum of adult patients and volunteers after the injection of procaine penicillin in arachis oil with 2% of aluminium stearate has been studied by the authors at the Sheffield Royal Infirmary. The serum penicillin level was estimated by comparing the effect of serial dilutions in phenol-red–glucose–serum medium upon *Streptococcus pyogenes* with that of similar dilutions of standard penicillin.

After a single injection of 300,000 units, the maximum concentration of penicillin in the serum was reached in about 3 hours, and a bacteriostatic level of more than 0·06 unit per ml. was maintained for 24 hours in 9 out of 10 cases. In 2 patients with impaired renal excretion a level of 2 to 4 units per ml. was found at the third hour. A further 33 patients received a single dose of 600,000 units, and in all cases the serum penicillin level was maintained above 0·06 unit per ml. for 24 hours and above 0·03 for 48 hours. Even after 72 hours the level in 24 out of 29 patients remained above 0·03 unit per ml., and the average for the whole group was above 0·06. Three patients were given 600,000 units of crystalline penicillin G in aqueous solution for comparison; the serum level fell below 0·03 unit per ml. in 10 hours. Daily doses of 600,000 units of procaine penicillin with 2% aluminium stearate were then given for 4 days to 15 patients: an almost constant serum penicillin level of 0·125 to 0·5 unit per ml. was maintained during treatment. The most constant levels were found when preparations containing the penicillin in particles less than 5μ in diameter were used. When caronamide (4 g. every 4 hours) was also given (in one case), the blood concentration of penicillin attained was higher than with the penicillin preparation alone.

The authors review the arguments for and against the discontinuous administration of large doses of penicillin and conclude that the balance of evidence is in favour of maintaining a steady blood level, such as that given by daily doses of 600,000 units of procaine penicillin with 2% aluminium stearate. Single daily doses also save time in nursing and cause less discomfort to the patient. A daily " peak " concentration may be superimposed upon the steady blood level by adding soluble penicillin to the injection if desired.
L. G. Goodwin

2440. **Oedema and Potassium Loss in Combined Sodium *p*-Aminohippurate and Penicillin Therapy. A Metabolic Study**
J. E. CATES. *Clinical Science* [*Clin. Sci.*] **8**, 53–63, 1949. 2 figs., 26 refs.

Sodium *p*-aminohippurate was used to enhance levels of penicillin in the treatment of bacterial endocarditis. This caused oedema, muscular weakness, alkalosis, and a low serum potassium. In a subsequent study of the effects of sodium *p*-aminohippurate on metabolism it was found that the body retained sodium and lost potassium. The significance of these findings is briefly discussed.—[Author's summary.]

2441. **Penicillin in Tissue Exudates after Injection**
J. UNGAR. *Lancet* [*Lancet*] **1**, 56–59, Jan. 14, 1950. 7 refs.

The amount of penicillin estimated to be present in the blood stream during treatment is sometimes insufficient to account for its therapeutic efficacy. Moreover, after severe tissue damage the drug can be detected in a wound longer after injection than in the blood. The author has studied the distribution of penicillin in diseased tissues and blood after single doses in animals. Artificial oedema was produced in the muscle tissue of rabbits' hind legs by the injection of turpentine, penicillin was given, and blood and oedema fluid were

withdrawn at intervals for penicillin assay. Doses of 30,000 units of penicillin were injected intramuscularly in aqueous solution, suspended in oil and beeswax, and as procaine penicillin. Higher doses (up to 100,000 units) did not prolong presence of the drug in the blood, but resulted in higher levels in the exudate.

No detectable amount of penicillin was found in any organ, but concentrations of 0·5 to 0·25 unit per ml. at 3 hours and of 0·25 to 0·06 unit per ml. at 5 hours were found in the exudate in the damaged muscle. After the injection of penicillin G (and of penicillin F plus dihydropenicillin F) a detectable level was present in the blood for 2 to 3 hours, whereas penicillin K could not be detected after 2 hours. The same relation held for penicillin levels in the exudate, as penicillin G could be detected up to 8 hours, a mixture of penicillins F and dihydro F up to 6 hours, but penicillin F only up to 2 hours after injection. Thus with small amounts of turpentine, injected intramuscularly, as a means of obtaining frequent samples of sterile exudate, detectable amounts of intramuscular penicillin remain in the fluid of damaged tissue about twice as long as in the blood stream. The therapeutic effect of large single doses may be attributed to prolonged accumulation in the inflamed tissue. *Malcolm Woodbine*

2442. **Location of Radioactive Penicillin in *Staphylococcus aureus* after Contact with the Drug**
P. D. Cooper, D. Rowley, and I. M. Dawson. *Nature* [*Nature, Lond.*] **164**, 842–843, Nov. 12, 1949. 1 fig., 5 refs.

TOXICOLOGY

2443. **Pneumonia in Children Following the Ingestion of Petroleum Products**
C. H. Heacock. *Radiology* [*Radiology*] **53**, 793–797, Dec., 1949. 4 figs., 4 refs.

During a period of 3½ years 156 children, whose average age was 19 months, were admitted to the John Gaston Hospital, Memphis, Tennessee, suffering from the effects of swallowing kerosene (paraffin) or similar products. There was one fatal case. The amount taken was generally small—usually "one swallow"—and this set up considerable coughing and choking, with a burning sensation in the mouth and throat and substernal pain, and was followed by epigastric pain and vomiting and, in some cases, subsequent cerebral depression and coma.

In 103 of the children there were some toxic symptoms, and 68 of these developed signs of pneumonia. The author considers that this resulted from inhalation of the oil during the spasm on swallowing. The post-mortem examination in the one fatal case revealed a haemorrhagic oedema of the lungs. Radiography of the chest in 60 of the cases showed abnormalities ranging from haziness of the lung fields to bronchopneumonic mottling of the regional type and more extensive consolidation of an entire lobe. There were no complications, and this is attributed by the author to the giving of chemotherapeutic agents to prevent the superimposition of bacterial infection upon the clinical pneumonia. *A. M. Rackow*

2444. **Use of Lithium Salts as a Substitute for Sodium Chloride**
J. H. Talbott. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 1–10, Jan., 1950. 18 refs.

The use of lithium chloride as a substitute for sodium chloride in salt-free diets was investigated. It is considered that an ideal substitute for sodium chloride should be indistinguishable from it in taste, should be non-toxic, should be capable of addition in the same form as table salt, and should not be destroyed by cooking or heating. Various toxic reactions have been described following the use of lithium salts but these are considered to be due to the sodium-chloride deficiency or other factors such as the presence of debilitating disease or administration of mercurial diuretics or digitalis. In other cases of alleged lithium intoxication the patients had been consuming much larger quantities of lithium salts than the author has found necessary. He has not observed untoward reactions with a serum lithium concentration under 1 milliequivalent. *Alan Kekwick*

2445. **Sodium Succinate—An Analeptic for Barbiturate Poisoning in Man**
R. H. Barrett. *Annals of Internal Medicine* [*Ann. intern. Med.*] **31**, 739–749, Nov., 1949. 10 refs.

The possibility of using sodium succinate as an antidote in barbiturate poisoning was suggested in 1943 as a result of animal experiments. In a controlled clinical trial in cases of thiopentone overdosage succinate definitely shortened sleeping time.

The effect of the drug in 15 cases of barbiturate poisoning (produced accidentally or with suicidal intent) has now been studied. Sodium succinate was given intravenously, but there was no fixed dose; the first 3 to 5 ml. of the solution (disodium succinate hexahydrate, 30%) was injected rapidly and the remainder given more slowly. If the initial dose was adequate, the patients coughed between the rapid and slow injections; a crimson flush appeared and a typical increase in respiration rate was noted. The slow intravenous injection was continued until definite analeptic responses were evident. Up to 42 g. of the agent has been given within 20 minutes, although the general dose was about 6 g. (20 ml. solution). The author observed no untoward effects from the use of sodium succinate in man. Its actual mode and site of action as an analeptic in barbiturate poisoning have not been determined. It is possible that tissue respiration is affected, though stimulation of reflexes may be an additive action. *G. B. West*

2446. **Acute Barbiturate Poisoning Treated by Intravenous Amphetamine (Benzedrine) Sulfate: Case Report**
W. D. Mayer and M. R. Beitman. *Harper Hospital Bulletin* [*Harper Hosp. Bull.*] **7**, 311–313, Nov.–Dec., 1949. 5 refs.

A 32-year-old woman patient was in deep coma 3½ hours after ingesting 45 grains (3 g.) "sodium

amytal ". A first dose of 20 mg. amphetamine sulphate was slowly given intravenously and immediate gastric lavage performed. A moderate laryngospasm was relieved by subcutaneous injection of $\frac{1}{150}$ grain (0·4 mg.) atropine sulphate. Ten-mg. doses of amphetamine sulphate in 5 ml. of water were given 20 minutes later and at 30-minute intervals. A rise in blood pressure and increase in depth of respiratory excursion and muscular response to stimuli followed each injection. The patient began to wake up 12 hours after admission and the drug was then given hourly in 30-mg. doses until treatment concluded at the 25th hour, when a total of 610 mg. had been given without any toxic reactions. Her gait was more steady and speech, though slurred, was coherent. In the subsequent 12 hours the mind cleared completely and the patient was considered to be fully recovered on the third day after admission.

Malcolm Woodbine

2447. **Fatal Results of Vitamin-D_2 Treatment in a Case of Erythema Induratum (Bazin's Disease).** (Vigantol-behandlung eines Erythema induratum Bazin mit tödlichem Ausgang)
R. M. BOHNSTEDT and F. PRINZ. *Strahlentherapie* [*Strahlentherapie*] **80**, 389–398, 1949. 3 figs., 33 refs.

A 52-year-old woman suffering from Bazin's disease received 120 mg. of " vigantol " (vitamin-D_2 concentrate) over a period of 4 weeks. There was good local response, but after 7 weeks the condition recurred and a second course of treatment was started. After 65 mg. of vigantol had been given the patient complained of anorexia, malaise, and vomiting. There were marked loss of weight, constipation, and recurrent bouts of pyrexia with rigors. The patient died within 2½ months from uraemia and activation of pulmonary tuberculosis, confirmed by post-mortem examination. The authors discuss these serious effects of vitamin-D_2 treatment.

G. W. Csonka

2448. **Diazomethane Poisoning: Report of a Fatal Case with Autopsy**
E. B. LEWINN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **218**, 556–562, Nov., 1949. 6 figs., 12 refs.

The author reports what he states to be the second case of diazomethane poisoning on record. Diazomethane is a very unstable, odourless, yellowish gas used chemically as a methylating agent. Because of its high degree of chemical activity it is generally employed dissolved in ether or benzene. The patient was a 28-year-old research chemist, engaged in an investigation in which diazomethane was involved. He accidentally inhaled the gases produced in his experiment, before which he had eaten some rather greasy food, which might have some significance on account of the fat solubility of the chemical. He soon developed a dry, persistent cough. The next day he also complained of fatigue and soreness behind the sternum, while his temperature had risen to 102·4° F. (39·1° C). Two days after the exposure there were signs suggestive of inflammatory changes in the lungs. The temperature remained elevated and cyanosis developed. On the fourth day the blood pressure started to rise and reached 180/90 mm. Hg after 12 hours. The pulse rate increased to 176, while the respiration rate was 44. Death occurred 100 hours after exposure. Terminal manifestations included mental confusion, muscular twitching, and a small haematemesis. Apart from an initial leucocytosis of 11,300 (polymorphonuclears 83%) rising to 23,600 per c.mm., laboratory examinations showed the presence of albuminuria with casts, and perhaps some degree of hyperglycaemia. At necropsy the findings were: acute ulcerative tracheo-bronchitis, bronchiolitis, and bronchopneumonia; toxic changes in heart, kidney, and liver; acute oesophagitis, gastritis, and duodenitis; and microscopic foci of necrosis in the brain with thrombosis in small blood vessels. The author considers the changes in the respiratory tract to be due to direct contact with the inhaled gas, while those in the upper alimentary tract were possibly caused by the diazomethane-contaminated sandwich. He points out that the patient never complained of dysphagia.

R. Salm

2449. **Toxic Effects of Antithyroid Drugs**
J. P. PETERS, E. B. MAN, D. M. KYDD, W. W. ENGSTROM, and L. L. WATERS. *Yale Journal of Biology and Medicine* [*Yale J. Biol. Med.*] **22**, 139–179, Dec., 1949. 11 figs., 47 refs.

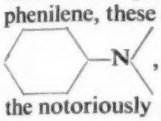
The authors describe the toxic effects of thiourea, the drug with which they have had most experience, and which they consider to be the most effective sulphur-containing antithyroid drug, weight for weight. In 300 cases treated for periods of up to 4 years they observed no agranulocytosis or significant leucopenia. Twelve case histories are given in detail, including those of 5 fatal cases with post-mortem findings. The vomiting and febrile reaction due to thiourea they found to be self-terminating; it was not necessary to discontinue the drug because of this. Urticaria was caused by the drug in one case. The precipitable iodine content of serum occasionally rose to unexpectedly high levels in patients showing toxic symptoms but whose thyrotoxicosis was well controlled. In several cases a febrile disorder was accompanied by arthritis and ulcers on the extremities and in the mouth; these patients were all over sixty.

G. S. Crockett

2450. **Agranulocytosis During Therapy with the Antihistaminic Agent Methaphenilene (Diatrin)**
T. G. DRAKE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **142**, 477–478, Feb. 18, 1950. 4 refs.

The case is reported of a man aged 81 suffering from chronic hypertrophic rhinitis and bronchitis, who developed agranulocytosis after 8 weeks' treatment with 8-hourly doses of 50 mg. of methaphenilene hydrochloride (" diatrin "; N, N-dimethyl-N^1-phenyl-N^1-(2-thenyl) ethylenediamine hydrochloride)—an antihistaminic drug homologous with tripelennamine hydrochloride (" pyribenzamine "). The leucocyte count fell to 1,000 per c.mm. (all the cells being lymphocytes) and the patient became critically ill, but with repeated

blood transfusions and the administration of aureomycin followed by a combination of penicillin and dihydrostreptomycin he recovered, his blood picture returning to normal some 14 days after the last dose of methaphenilene. The sternal marrow, examined towards the end of this period, showed marked depression of the granulocyte series.

The author has only been able to find mention in the literature of 4 other cases of agranulocytosis associated with antihistaminic therapy, the drugs concerned being tripelennamine in 3 of these and " 2339 RP " in the fourth. He points out that, in common with methaphenilene, these drugs contain the " benzamine " linkage,  , which also forms part of the structure of the notoriously granulocytopenic drug, amidopyrine.

D. I. Crowther

2451. **Intoxication Due to *Cicuta virosa*.** (Vergiftiging door waterscheerling (*Cicuta virosa* L.))
D. P. R. KEIZER. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 2811–2812, Aug. 13, 1949. 2 refs.

In three children 4, 3, and 4 years of age respectively, a very severe clinical picture, including coma and convulsions, developed after ingestion of the root of the water hemlock, *Cicuta virosa*. One child died. Treatment was purely symptomatic in the absence of a specific antidote.

E. Kits van Waveren (*Excerpta Medica*)

2452. **Bromide Intoxication. Report of 36 Cases**
J. D. CAMPBELL. *Southern Medical Journal* [*Sth. med. J.*] **42**, 967–973, Nov., 1949. 16 refs.

The first case of bromide intoxication was reported by Huette in 1850, soon after the introduction of the drug into medicine, and although since then there have been many reports of mental disturbance due to bromides the drug continues to be sold almost without regulation in the U.S.A. Chemists and doctors are not sufficiently alert to the dangers of this " mild sedative ". The author gives details of 36 patients (26 women and 10 men) who were suffering from bromide intoxication. Amongst them were 20 cases of manic-depressive psychosis (18 depressive and 2 manic), 4 of psychoneurosis (with alcoholism added in 2 of these), and 4 of involutional psychosis; 2 patients had had head injuries and were unable to sleep, 2 were homosexuals, and one was an epileptic who had been taking bromides for 20 years. The author warns against the common belief that a concentration of bromide in the blood of 150 mg. per 100 ml. is necessary to produce psychotic symptoms; he has seen such symptoms when the blood bromide level has been as little as 36 mg. per 100 ml. He also states that too few physicians consider bromism as a diagnosis when a rash is not present; the latter is due to idiosyncrasy and may be absent when the drug has been taken for long periods. Of a large number of proprietary preparations listed, the majority contain 10 to 15 gr. (0·65 to 1 g.) of bromide in each dose.

In the treatment of bromide intoxication, the too hasty administration of sodium chloride often aggravates the mental symptoms owing to the increase produced in circulating bromide; the author therefore gives normal saline intravenously with salt tablets orally, and finds this very satisfactory; paraldehyde (5 to 8 ml.) is the sedative of choice if necessary. *T. E. C. Early*

2453. **Niacinamide in Bromide Intoxication**
R. S. HARRIS and P. S. DERIAN. *Southern Medical Journal* [*Sth. med. J.*] **42**, 973–978, Nov., 1949. 9 refs.

The authors quote the work of Axelrod, Handler, and Featherstone, and others in stating that nicotinic acid and its derivatives are used in the formation of coenzymes I and II and that it is presumably a deficiency in these oxidative systems which produces the symptoms of pellagra. Pellagra and bromism are known to have similar symptoms—neurological (tremors, headaches, and spastic gait), psychiatric (hallucinations, depression, and disorientation), dermatological (ranging from roughened skin to bullous eruptions), oral, and gastrointestinal. As a working hypothesis, therefore, the authors assumed the destruction, or faulty synthesis, of these enzymes as a result of a rise in bromide level in the blood. Three groups of dogs were studied, one being given a diet deficient in nicotinic acid (to the point of inducing black tongue), the second being given a basal diet and sufficient sodium bromide to maintain a serum bromide level of 300 mg. per 100 ml., and the third the same with the addition of nicotinamide (10 mg. per kg. body weight daily). The first group developed diarrhoea after about 28 days, ataxic gait after 35 to 42 days, and inflammation of the tongue after 29 days; the second group developed similar lesions much sooner, while in the third group the dogs seemed capable of tolerating a blood bromide level of 300 mg. per 100 ml. without the appearance of signs or symptoms.

A group of 6 patients with bromism were treated concurrently with 600 to 750 mg. of nicotinamide daily, 2 being given the conventional salt therapy in addition. All 6 patients were devoid of neuropsychiatric symptoms 3 to 5 days after starting treatment, there being no apparent advantage in giving salt, which is contraindicated in hypertension, nephritis, and other conditions.

T. E. C. Early

2454. **Acetaldehyde and the Metabolism of Ethyl Alcohol.** (L'acétaldéhyde et le métabolisme de l'alcool éthylique)
R. LECOQ. *Thérapie* [*Thérapie*] **4**, 177–181, 1949. 14 refs.

Tetraethyl thiuramdisulphide (" antabus ") is now being widely used in the treatment of alcoholism; after its administration the taking of even small amounts of alcohol produces the most unpleasant symptoms. The author's experiments do not support the view that these symptoms are due to the accumulation of acetaldehyde. He found in the rabbit that the intramuscular injection of 15 mg. of nicotinamide and 25 mg. of adenine 30 minutes beforehand greatly reduced the toxic effects of alcohol even when it was given together with 0·5 g. of antabus, whereas this treatment did not prevent the

induction of epileptiform convulsions by an intravenous dose of acetaldehyde (5 ml. of a 5% isotonic solution). It is presumed that the giving of these vitamins hastens the destruction of some other toxic product of the metabolism of ethyl alcohol. *F. N. Fastier*

2455. **Researches into the Mechanism of Action of Certain Substances Advocated for the Treatment of Chronic Alcoholism.** (Recherches sur le mécanisme d'action de quelques substances préconisées dans le traitement de l'alcoolisme chronique)
R. Lecoq, P. Chauchard, and H. Mazoué. *Thérapie* [*Thérapie*] **4**, 182–195, 1949. 32 refs.

In experiments on white rats, the effect of alcohol and of certain drugs used in the treatment of alcoholism on the chronaxie of peripheral nerves was studied [very few details of technique are given]. Alcohol alone (1 ml. of a 25% solution by subcutaneous, oral, or rectal route) caused a slight, temporary decrease in chronaxie followed by a much larger and more persistent increase. The effect of alcohol was exacerbated when 5 or 10 mg. of tetraethyl thiuramdisulphide ("antabus"), apomorphine (5 mg.), or primary octyl alcohol (50 μg.) was injected at the same time or, preferably, 20 to 60 minutes beforehand. These three drugs are thought to produce a distaste for alcohol because they cause symptoms due to an abnormally high concentration of its toxic metabolic products. On the other hand, administration of nicotinamide and adenine beforehand minimized the effect of alcohol on nerve chronaxie; such drugs are regarded as true detoxicants for ethyl alcohol (see Abstract 2454). Potassium thiocyanate and phenyl-1-amino-2-propane, given a few minutes before or together with a test dose of ethyl alcohol, were also found to counter the nervous depression normally produced by alcohol alone, but the amounts given had to be strictly controlled. *F. N. Fastier*

2456. **The Treatment of Alcoholism with "Antabus".** (Le traitement de l'alcoolisme par l'antabuse)
V. Aitoff. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris.*] **25**, 4033–4040, Dec. 30, 1949. 9 refs.

"Antabus", tetraethyl thiuramdisulphide, was employed in 10 cases of alcohol addiction. Seven of the patients are regarded as cured and 2 as much improved; in only one case did the treatment fail. All the cases were treated without admission of the patient to hospital; this is, however, only possible with active co-operation on the part of the patient and his relatives. The habitual intake of alcohol must be stopped 2 days before the start of antabus medication and during the course of treatment no alcohol, or only very little, is allowed. On the first day, with breakfast, 1 g. of antabus is given, on the following few days 0·5 g. and then, in rapidly decreasing daily dosage, 0·25 g., 0·12 g., and 0·06 g. The duration of the full course of treatment depends on the individual patient's reactions, but at least 6 months seems to be required, and for another 6 months the patient should be kept under observation. After the first 3 days of treatment a control test is carried out, the test being repeated weekly for the next 3 weeks and every 3 to 4 weeks later. In the presence of the doctor the patient drinks the equivalent of 10 to 20 ml. alcohol. If he has taken antabus regularly the reaction becomes evident in 5 to 10 minutes: the face, and sometimes the upper part of the body, is intensely flushed, and palpitations and mild dyspnoea follow. With larger doses of alcohol sickness and vomiting may develop. These symptoms, usually accompanied by headache, are very unpleasant but disappear within a few hours, leaving the patient sleepy. The patient is advised to provoke such reactions at home once weekly in the presence of one of his family in order to create an aversion to alcoholic drinks. To avoid dangerous reactions a careful physical and mental examination of each case before treatment is advisable, and particular caution is necessary in persons with organic disorders. In such cases admission to hospital is preferable. *F. F. Kino*

2457. **Employment of a Substance [Magnesium Thiosulphate] to Prevent Severe Toxic Episodes in the Treatment of Alcoholism with "Antabus".** (A propósito do tratamento do alcoolismo pelo antabus (tetraetiltiuramdisulfida) e de uma substância destinada a prevenir acidentes tôxicos graves no decurso do tratamento)
E. Arruda. *Neurobiologia, Recife* [*Neurobiologia, Recife*] **12**, 267–276, Sept., 1949. 3 refs.

2458. **The Addiction Liability of Some Derivatives of Meperidine**
H. Isbell. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 182–189, Oct., 1949. 3 figs., 20 refs.

2459. **Carbon Tetrachloride Poisoning in Man. I. The Mechanisms of Renal Failure and Recovery**
J. H. Sirota. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 1412–1422, Nov., 1949. 1 fig., 32 refs.

2460. **Fatal Poisoning of an Infant by Anti-anaemic Pills Containing Iron, Manganese, and Copper**
J. H. Prain. *British Medical Journal* [*Brit. med. J.*] 1019–1020, Nov. 5, 1949. 4 figs., 7 refs.

2461. **The Toxicity of Methyl and Ethyl Acrylate**
J. F. Treon, H. Signon, H. Wright, and K. V. Kitzmiller. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **31**, 317–326, Nov., 1949. 5 refs.

THERAPEUTICS

2462. **Anticoagulant Therapy**
H. W. Fullerton and G. Anastasopoulos. *British Medical Journal* [*Brit. med. J.*] **2**, 1492–1495, Dec. 31, 1949. 4 figs., 9 refs.

After an introductory section on the merits of, and the difficulties caused by the use of, heparin and dicoumarol, this paper deals with methods of measuring "accelerated clotting time" ("prothrombin time") and with the effects of different factors on it. The Morawitz theory of blood clotting, modified by assumption that there is a lipid factor in addition to the classical trio of thrombo-

kinase, ionized calcium, and prothrombin, is accepted, so that four variables control the speed of blood coagulation. The methods in use to-day are those of Quick, with rabbit brain as the source of thrombokinase, of Fullerton, in which Russell viper venom is used for the same purpose, and a modification of the last, in which ovolecithin is added (an aqueous solution is preferred to the alcoholic one recommended by Witts and Hobson). In all methods, calcium is added, so that this variable is excluded. When venom is used with lecithin, the thrombokinase and lipid factors are excluded, leaving prothrombin as the only variable to be measured; variations in the plasma lipid level are not shown. The present experiments showed that, with brain alone, the amount of lipid factor is adequate but that of thrombokinase is suboptimal. Quick's test also fails to reveal variations in the plasma lipid level, and, as the amount of thrombokinase is suboptimal and varies from one preparation to another, the method should be superseded by the venom with lecithin test. With venom alone, the prothrombin time would be accurately measured only if the plasma lipid level were adequate.

Further experiments showed that, if a state of alimentary lipaemia was induced, the results with venom and lecithin or with the Quick method were unchanged, but if venom alone was used the prothrombin time became progressively shorter with the absorption of fat, reaching after 4 hours the same figure as in the venom and lecithin test. In patients in whom the prothrombin level had been lowered by dicoumarol alimentary lipaemia was less effective and might fail to reduce the clotting time with venom alone. It is suggested that a rise in the plasma lipid level accompanies the reduction in prothrombin time. To obtain confirmation, the authors measured the clotting time with venom alone and with venom and lecithin in patients from the start of dicoumarol treatment. At first, the time with venom alone was about double that with venom and lecithin, but after 10 days they were about equal. The authors point out the need, when venom is used alone, for the rigid exclusion of haemolysis, as even the slightest amount shortens the prothrombin time, probably because of the lipid fraction of the erythrocyte envelope.

They conclude that the prothrombin reduction, but not the coagulability of the blood, can be measured by the venom with lecithin method, whereas the venom test alone will measure the latter but not the former. They advise the simultaneous use of both tests.

Reginald St. A. Heathcote

2463. **Replacement Transfusion Following Administration of Incompatible Blood. Report of Case with Successful Outcome**

J. E. Conley, J. Erbes, F. J. Stoddard, and J. W. Frye. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 1131–1134, Dec., 1949. 4 refs.

A woman whose blood was of group O was transfused during operation for a ruptured Graafian follicle cyst with 500 ml. of blood of group AB. This was followed by a fall in blood pressure, and further infusions of 2,000 ml. dextrose–saline and 500 ml. of group-O blood were given. Ten hours later 200 ml. of blood-stained urine was withdrawn by catheter. A further 2 litres of intravenous fluid (sodium lactate and glucose) was given. At the 16th hour, after only 400 ml. of urine had been collected, a replacement transfusion (5,000 ml. of blood removed, 6,000 ml. infused) was undertaken. In the following 6 hours 2,200 ml. of clear urine was obtained. There was no further disturbance of urinary excretion. Reasons are given for suggesting that the replacement transfusion altered the final course of the condition.

John F. Loutit

2464. **The Effects of Micro-waves. A Preliminary Investigation**

A. C. Boyle, H. F. Cook, and T. J. Buchanan. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **13**, 2–9, Jan., 1950. 7 figs., 10 refs.

In their introduction the authors discuss the nature and action of micro-waves and describe the design of a typical 10-cm. radar set which will minimize loss of energy by reflection from the tissues. This improvement facilitates the more accurate measurement of actual energy passing from the applicator into the body, and also permits the use of a lower power output (30 to 100 watts) than has previously been necessary.

They then describe the effects of over-dosage on laboratory animals treated with micro-waves at a power level of 8 watts for 5 minutes, which produced local coagulation necrosis in the skin, subcutaneous tissue, and superficial muscles. In observations on the effect of a metallic foreign body in the field of irradiation, evidence was found of coagulation necrosis in the adjacent muscles. With the present apparatus the heating effect is confined to the first few centimetres below the skin, micro-waves being more penetrating than radiant heat, but much less so than short-wave diathermy.

The authors are of the opinion that micro-wave therapy will not replace short-wave diathermy in the treatment of large areas or deep-seated lesions, but may have a place in the treatment of more superficial conditions such as ophthalmic conditions, sinusitis, and localized septic lesions.

M. H. L. Desmarais

2465. **Ultrasonics in Medicine**

P. A. Nelson, J. F. Herrick, and F. H. Krusen. *Archives of Physical Medicine* [*Arch. phys. Med.*] **31**, 6–19, Jan., 1950. Bibliography.

The purpose of this paper is to acquaint the practising physician with certain medical aspects of ultrasonics, and to provide a bibliography useful to those interested in research in ultrasonics.

Unlike electromagnetic vibrations, sonic and ultrasonic waves require some material medium for their propagation, but they behave in some ways like light waves. Ultrasonic waves cause, by virtue of their high-frequency vibration, profound biological effects such as the disruption of plant cells and protozoa and the haemolysis of erythrocytes. They have bactericidal and virucidal effects, and their use has been applied experimentally to the control of infections. Experiments have been carried out on the effect of ultrasonic waves on

malignant tumours, but the conflicting reports of different authors make their use as yet unjustifiable when this might delay the institution of other, proved methods of treatment. Claims of improvement and cure by means of ultrasonic therapy have been made by many authors, mainly from the continent of Europe, in such varied conditions as inflammatory lesions, deformities, and skin conditions. These reports are for the most part based on clinical impressions and not on truly scientific, controlled experiments. However, in view of the many claims made, further fundamental research is necessary to ascertain the true diagnostic and therapeutic value of ultrasonic waves. *M. H. L. Desmarais*

REPELLENTS AND INSECTICIDES

2466. **Observations and Studies on the Sphere of Activity of the New Repellent, " Kik-Geigy ".** (Beobachtungen und Untersuchungen über den Wirkungsbereich des neuen Repellent " Kik-Geigy ".)
R. WIESMANN and R. LOTMAR. *Acta Tropica* [*Acta trop., Basel*] **6**, 292–349, 1949. 22 refs.

The preparation " kik " consists of a mixture of various chemical substances, each with an insect-repellent action. Kik is applied to exposed skin surfaces and is effective for 4 to 10 hours against various mosquitoes. Against several species the effect is diminished when the treated skin is covered, as by a stocking. The repellent action was tested under laboratory and field conditions on various insects and other arthropods. The duration of the repellent action was considered satisfactory against many mosquitoes (*Anopheles quadrimaculatus* excepted) and one or more species of flea, bed-bug, gad-fly, and tick (*Ixodes ricinus*, young larvae only). The repellent action was not so satisfactory against *Musca domestica*, *Stomoxys calcitrans*, *Glossina palpalis*, *Pediculus vestimenti*, and *Rhodnius prolixus*. Most of the insects listed above appeared to be repelled by the smell of kik ; *Rhodnius*, however, was only slightly affected, while bed-bugs and body lice did not react at all to the vapour. Experiments with *Musca* and *Stomoxys* suggested that the antennae are concerned in the perception of smell. All the insects showed signs of " shock " after direct tarsal contact with the repellent, and tended to crawl away from it.

W. H. Horner Andrews

2467. **Diethyl-*p*-nitrophenylthiophosphate: A New and Effective Insecticide.** (Diäthyl-*p*-nitrophenylthiophosphat, ein neues Schadlingsbekämpfungsmittel)
M. SPINDLER. *Praxis* [*Praxis*] **38**, 936–939, Oct. 20, 1949. 24 refs.

As DDT is not effective against all insects, other compounds have been tested, especially the organic derivatives of phosphoric acid. Diethyl-*p*-nitrophenylthiophosphate (" parathion ") is one of the most promising. It is toxic to higher animals, though the lethal dose depends on sex, season, and other factors. The lethal action is not caused by interference in carbohydrate metabolism, but by blocking of cholinesterase. The symptoms are similar to those of muscarine—stimulation of parasympathetic action. Atropine and papaverine are of therapeutic value in cases of poisoning, and " parpanit " is especially useful. As intake by the skin is very easy, the latter must be washed with hot water and soap in all cases of poisoning. Skin lesions are absent or negligible.

P. J. Van der Lee (*Excerpta Medica*)

2468. **DDT and Gammexane as Residual Insecticides Against *Anopheles gambiae* in African Houses**
R. C. MUIRHEAD-THOMSON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **43**, 401–412, Jan., 1950. 2 figs., 6 refs.

Anopheles gambiae is the most important vector of malaria in Africa, and its control represents a problem of primary importance in tropical medicine. Following the introduction of the new insecticides it was at first believed that residual spraying with DDT provided a satisfactory solution, but later work by a number of independent investigators proved that this view was far too optimistic, and that the reduction in density of the species observed in treated houses was largely the result of the repellent action of the DDT. In addition it was shown that this repellent action was not sufficient to prevent the *A. gambiae* from entering the houses and feeding on the occupiers. Trials with benzene hexachloride (B.H.C.) preparations have not been as extensive as those with DDT, but they have yielded evidence to support the view that " gammexane " is less repellent to this species than DDT; although less persistent, gammexane destroys a higher proportion of the *A. gambiae* that enter treated dwellings.

The experiments described in this paper were carried out at Dar-es-Salaam in experimental native houses provided with window traps which captured most of the mosquitoes entering the houses and subsequently trying to escape. The author summarizes the results as follows: " In huts treated with DDT water dispersable powder at the rate of 400 mg. DDT per square foot [4,300 mg. per sq. m.] (twice the normal dose), numbers of gambiae can feed in the treated hut and escape alive. Of those that leave the treated hut at least 98% are alive after 24 hours, and at least 80% after 48 hours. The number of *A. gambiae* found dead inside the treated hut is only about 1% of those that escape alive after feeding. Attempts to increase the kill by screening window openings have met with only limited success.

" Similar huts treated with B.H.C. in the form of ' gammexane ' dispersable powder, P. 530 at the rate of 24 mg. gamma isomer per square foot [258 mg. per sq. m.], have proved completely lethal to all gambiae entering for at least 13 weeks after treatment. During that time there is no indication of any gambiae escaping unharmed from the hut. The number of dead blood-fed and unfed gambiae found regularly on the floor sheets is proof of continued lethal action for at least 3 months after treatment. The superiority of gammexane over DDT in control of *A. gambiae* is so clearly marked that it is the obvious insecticide on which to concentrate."

R. M. Gordon

Radiology

2469. **Late Injuries from Thorotrast, Estimated from the Oldest Known Case of Thorotrast Injury.** (Die Spätschäden des Thorotrasts, beurteilt nach dem ältesten, bisher bekannten Thorotrastschädensfall)
R. BIRKNER. *Strahlentherapie* [*Strahlentherapie*] **78**, 587–608, 1949. 18 figs., bibliography.

Materials used in contrast radiography have well-defined toxic effects and cause secondary radiation on subsequent diagnostic radiography, thorotrast being especially dangerous; 100 ml. of this preparation contains radioactivity equivalent to the radiation from $1{\cdot}24\times10^{-6}$ g. of radium. Excretion is slow and the presence of thoratrast has been reported 5½ years after arteriography. The author reviews the literature on immediate and late toxic effects. Studies in animals are also discussed.

A case is reported in which hepato-lienography with thorotrast was carried out 17 years ago, before operative removal of echinococcal cysts of the liver A second operation for removal of another cyst was carried out 7 years later. During the past 6 years the patient has had pain in the right hypochondrium; 12 years ago oligomenorrhoea started and from this time there has been no pregnancy, although previously the patient had had 9 abortions. The patient is now aged 45. The liver is enlarged to the iliac crest and tender; the spleen is enlarged. The patient has a hyporegenerative anaemia with leucopenia. In the bone marrow there is an increase in immature erythroblasts. The granulocytes show marked toxic granulation and numerous macrophages containing small quantities of thorotrast are seen. Urobilin and urobilinogen in small quantities are present in the urine. There is a rise in the blood sugar level and the Takata-Ara reaction is positive.

An intravenous pyelogram and two cholecystograms revealed no abnormality. Other radiographic examinations revealed a large liver with large quantities of thorotrast. The main bile ducts were outlined by the same material. Deposits of thorotrast were also found in a midline shadow, in hilar, parabronchial, and abdominal lymph nodes, one lobe of the lung, and in the bronchi. The quantity of radiation present corresponded to 30% of the original amount of thorotrast injected. At this time the patient had a further exploratory laparotomy. A hard cylindrical mass was found attached to the liver. It was opaque to *x* rays and contained 2·048 g. of thorotrast (14% of the original amount). The mass was a non-inflamed collection of connective tissue with rich deposits of thorotrast. Some calcification was present and the liver itself showed cirrhosis. By the taking of 75 radiographs in 17 years the radiation dose to the liver was increased approximately ten times, the author calculates. Thorotrast deposits in the tissues may be so fine as to be invisible on radiographs. The author advises the complete withdrawal of thorotrast from diagnostic radiology. *W. J. Czyzewski*

2470. **Hyperheparinemia—the Cause of the Hemorrhagic Disease Produced by Total-body Exposure to Ionizing Radiations**
J. G. ALLEN, M. SANDERSON, M. MILHAM, A. KIRSCHON, and L. O. JACOBSON. *United States Atomic Energy Commission*, 1–33, Nov., 1946. 6 figs., 21 refs.

2471. **Can the Defence Mechanism of the Body be Influenced by Roentgen Irradiation? Report on a Preliminary Clinical Investigation of the Plasma or Serum Protein Pattern in Rheumatoid Arthritis**
H. NEY. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **8**, 191–204, Sept., 1949. 9 figs., 47 refs.

It was decided in an investigation of the biological effect of *x*-rays to determine in what way they might influence the natural resistance of the body to infection in rheumatoid arthritis. The scheme was to allow for variation in dosage and wave-length. The findings in the present paper refer to soft radiation given to the trunk.

On the assumption that the reticulo-endothelial system plays some part in the " natural defence mechanism of the body ", serum albumin and globulin values were chosen as an index of the state of body defence, in patients being irradiated. In this series of cases, where low albumin and high globulin levels were found, irradiation produced a return towards more normal figures. The albumin–globulin ratio has been found to be low in rheumatoid arthritis, and can be correlated with the general state of health. A return towards more normal values accompanies clinical improvement or arrest of the disease.

Reference is made to the part that allergy may play in the aetiology of rheumatoid arthritis. Little attention has been paid so far to the effects of soft radiation in desensitization or in inflammatory states, in spite of the innumerable investigations on *x*-ray therapy in every type of disease. Previous experience of this therapy in dermatology led the author to believe that it might prove a valuable therapeutic agent in other branches of medicine.

In the 9 cases reviewed treatment was carried out with a contact therapy set at 50 kV and 2 to 3 mA, with no added filter, a half-value layer of 0·3 mm. Al, and focus-skin distance of 56 cm. Wide-field irradiation with fields of 30×50 cm. was given anteriorly and posteriorly to the trunk in doses of 5 to 50 r once weekly (sum of anterior and posterior dose). Of the 9 cases treated, all of which had shown no previous response to other forms of treatment, 6 responded with clinical improvement, 2 did not respond, and one showed only temporary improvement. In the 3 cases not improved albumin–globulin ratios were normal or only slightly decreased, while in those responding albumin level fell and globulin level rose. Alteration in the serum proteins preceded a change in the clinical state.

Liver function tests revealed no abnormality in the 6 responding cases, but definite abnormality in the 2 non-responding cases and slight abnormality in the remaining case. *A. W. G. Goolden*

2472. **Transient Hemiplegia Associated with Cerebral Angiography (Diodrast)**
J. G. CHUSID, F. ROBINSON, and M. P. MARGULES-LAVERGNE. *Journal of Neurosurgery* [*J. Neurosurg.*] **6**, 466–474, Nov., 1949. 5 figs., 26 refs.

RADIOTHERAPY

2473. **On Roentgen Treatment of Intracranial Gliomas.** [In English]
A. ENGESET. *Acta Radiologica* [*Acta radiol., Stockh.*] **32**, 210–228, 1949. 3 figs., bibliography.

The literature concerning the radiological treatment and the surgical extirpation of gliomata is reviewed and the lack of success, particularly in the more undifferentiated tumours, is noted, although cerebellar medulloblastoma may form an exception in that several workers report some long-term survivals after radiation treatment. The experimental results, in animals, of the exposure of the brain to *x* rays and the recorded irradiation injuries in the human brain are briefly considered.

The author reports 39 cases of intracranial glioma treated by *x*-irradiation, in which biopsy had been performed. In most cases the tumour had been partly removed surgically before treatment with *x* rays. The average survival time in 18 cases of glioblastoma multiforme was 8 to 9 months. Of 12 cases of astrocytoma continuing survival is recorded in 8 for periods of 26 to 174 months, but with various neurological disabilities in all. One of 2 patients with astroblastoma survives at 70 months and 2 with oligodendrogliomata survived 48 and 54 months respectively. The survival of 4 patients who underwent operation and irradiation treatment for medulloblastoma was 17, 24, 30, and 137 months respectively, the last patient being still alive. Recent cases have been treated without operative intervention and the results are reported as encouraging. Six patients with tumours in the region of the pineal body or the third ventricle have been treated by Torkildsen by ventriculo-cisternostomy. Some have also received irradiation and in general these latter have survived longer.

A tumour dose of 5,000 r for gliomata is attempted, the daily fraction being kept low initially where no decompression has been performed. One case of brain necrosis due to irradiation is recorded. *G. Boden*

2474. **Radioiodine Therapy of Metastases from Carcinoma of the Thyroid: A Six-year Progress Report**
S. M. SEIDLIN, I. ROSSMAN, E. OSHRY, and E. SIEGEL. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **9**, 1122–1137, Nov., 1949. 10 figs., 5 refs.

From 1943 to 1949, 30 patients with metastases from carcinoma of the thyroid were studied at the Montefiore Hospital, New York. It was found that surgical or radiation thyroidectomy and administration of thyrotrophic hormone would sometimes induce uptake of radio-iodine in metastases which had previously shown no uptake. Twelve patients were treated with radio-iodine; 7 are living (the condition in 3 is greatly improved, in 2 moderately improved, and in 2 stationary) and 5 are dead (in 3 the condition initially improved with prolongation of life, in 2 it showed no improvement).

Details are given of a case observed for 6 years. Admitted in 1943 bedridden with multiple metastases and hyperthyroidism, the patient received a total of 111 mc. I^{130} and 397 mc. I^{131}. Myxoedema developed and thyroid administration was required. The patient can now move freely and he has no pain. No new metastases have appeared. The pulmonary metastases have disappeared, but the metastases in bone have shown no radiological change. Recently, one of the metastases in the skull was removed surgically after administration of a test dose of 10 mc. I^{131}. Section showed no viable tumour cells, but radioautographs showed a concentration of radio-iodine in some of the apparently necrotic tissue. The reason for this concentration of I^{131} is unknown, but it is suggested that the breakdown products of thyroid tumour cells may be capable of combining selectively with iodine, or that the reaction may be similar to the staining of amyloid by iodine and therefore independent of a thyroid origin. *G. Ansell*

2475. **The Treatment of Metastatic Thyroid Cancer with Radioactive Iodine: Credits and Debits**
J. B. TRUNNELL, L. D. MARINELLI, B. J. DUFFY, R. HILL, W. PEACOCK, and R. W. RAWSON. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **9**, 1138–1152, Nov., 1949. 11 figs., 7 refs.

At the Memorial Hospital, New York, 25 patients with metastases from thyroid carcinoma were studied. Nine patients were given therapeutic doses of I^{131}; in 4 of these there was definite improvement. The value of thyroidectomy (surgical or radiation) in inducing uptake of I^{131} in metastases is stressed. Administration of thyrotrophic hormone to one patient increased the uptake of I^{131} by the metastases without significantly increasing the uptake by normal thyroid tissue. After this, there was a refractory state for several weeks during which time the metastases collected no I^{131}. Thyrotoxic crises occurred in 3 patients. Subsequently these crises were prevented by administering thiouracil (1·5 g. daily) for several weeks, before giving the therapeutic dose of I^{131}. The administration of thiouracil also increases the capacity of the metastases to concentrate I^{131}. In one case with extensive metastases in the skull cerebrospinal-fluid pressure increased considerably after the administration of therapeutic doses of I^{131}.

All the patients given therapeutic doses showed temporary depression of one or more peripheral blood elements. Bone marrow biopsy in 7 patients revealed decrease in the total cell count and reversal of the erythroid–myeloid ratio. One patient died from a pancytopenia. Doses as small as 10 mc. I^{131} may produce an increase in the amounts of urinary and faecal coproporphyrins.

Three women under the age of 41 developed amenorrhoea. As there was no decrease in the urinary titre of follicle-stimulating hormone, it was assumed that the amenorrhoea was not due to pituitary irradiation. The authors were also unable to demonstrate any concentration of I^{131} by the ovaries of adult women. The amenorrhoea was probably due to ovarian damage from circulating I^{131}. *G. Ansell*

2476. **Rotation Treatment of Cancer of the Esophagus. A Clinical Material**
C. KREBS, H. NIELSEN, and P. E. ANDERSEN. *Acta Radiologica* [*Acta radiol., Stockh.*] **32**, 304–316, 1949. 1 fig., 28 refs.

A short account is given of a rotation technique for radiotherapy of cancer of the oesophagus. An analysis is made of 217 cases treated by this method, showing age and sex distribution, duration of symptoms, site of tumour, and histology. The period from onset of symptoms to admission to hospital was found to increase significantly with the distance of the tumour-site from the incisor teeth. The response to treatment showed a similar deterioration as the tumour-site approached the cardia.

While making modest claims for the curative results of rotation treatment (less than 2%), the authors emphasize the importance of this technique as a palliative procedure. Radiographic and clinical improvement has been considerable in many cases and the average duration of life has been doubled as compared with results obtained by previous cross-fire techniques and with published data. In more than 20% of cases, the primary tumour was histologically proved to be destroyed, although metastases ultimately killed the patient. Urging public education to reduce delay in treatment, the authors are hopeful for the future. *E. C. Easson*

2477. **Irradiation Treatment of Local Recurrence and Metastases of Carcinoma of the Breast after Operation.** (Über die Strahlenbehandlung von lokalen Recidiven und Metastasen beim operierten Brustkrebs)
R. BAUER. *Strahlentherapie* [*Strahlentherapie*] **78**, 527–532, 1949. 4 figs., 34 refs.

The general principles of radiotherapy in cases of recurrent or metastatic carcinoma of the breast after operation are discussed and the author stresses the value of post-operative prophylactic irradiation, which should be graded according to the pathological report on the excised material. The majority of recurrences are situated in or near the scar, while metastasis is most commonly to the supraclavicular lymph nodes or occasionally the deep axillary lymph nodes, with oedema of the arm in the latter case, of the same side as, or the opposite side to, the primary site. Close-range irradiation combined with tangential deep irradiation of the thoracic wall is recommended. Recurrences in the scar receive a large dose (5,000 to 6,000 r) without consideration of the skin, and nodular skin metastases receive 3,000 to 4,000 r. Skin necrosis heals well in a few weeks: out of 40 cases of necrosis, a bad response was obtained only in 2 cases, in both of which carcinoma tissue was found on biopsy and the skin healed well after further irradiation. The treatment of lymph-node metastases with deep *x* rays alone (with a half-value layer of 0·95 mm. Cu and total dose of 3,000 to 4,000 r, 200 r being given daily) is not so satisfactory. The majority of recurrences are in young women who are still menstruating. Good results were obtained with *x*-ray sterilization and the administration of testosterone. The occurrence of premenstrual discomfort of the breasts is considered to favour recurrence. *W. J. Czyzewski*

2478. **Wide Field Irradiation and the Platelet Count.** [In English]
W. M. COURT BROWN. *Acta Radiologica* [*Acta radiol., Stockh.*] **32**, 407–427, 1949. 17 figs., 7 refs.

The author presents the results of an investigation into the value of the platelet count in the control of wide-field *x*-ray therapy instead of the orthodox total leucocyte or lymphocyte count. With this method of treatment the leucocyte count is not always a reliable index of bone-marrow damage and fatal radiation anaemia may supervene although the count is within " safe " limits. Petechial haemorrhages were encountered shortly after the end of treatment and usually preceded manifest anaemia. When the latter did develop it was accompanied by marked thrombocytopenia.

The technique of platelet counting is described in an appendix. The normal range is 200,000 to 400,000 per c.mm., and 100,000 per c.mm. is regarded by the author as the probable lower limit of safety. In the majority of cases with normal haematopoiesis at the time of treatment, a double-peaked initial increase up to twice the pre-irradiation level follows within the first 10 days. Thereafter the platelet count falls exponentially. The calculated gradient of this fall was found to increase significantly with increase in the irradiated volume.

In cases with impaired haematopoiesis the gradient of platelet fall is much steeper and indicates a correspondingly lowered tolerance to radiation. The author emphasizes that total leucocyte and lymphocyte counts in such cases give no indication of this loss of tolerance. In this category he places cases of previous extensive irradiation and those of neoplastic involvement of the bone marrow, including the chronic leukaemias and aleukaemic reticuloses.

In the majority of cases the author admits that the total leucocyte and platelet counts fall together to their acknowledged safety levels (2,000 and 100,000 per c.mm. respectively). In a second minority group the total count falls more rapidly than the platelet count to, or even below, the safety level, and a case is cited where satisfactory regression of a sensitive tumour might not have been obtained had not the finding of an adequate platelet count led to a confident continuation of treatment.

It is claimed that there is no consistent pattern of lymphocyte response to radiation. Radiation anaemia may develop even where lymphocyte levels are maintained above the 300 per c.mm. " safe " level; in other cases, provided the platelet level is maintained, anaemia has not ensued even with lower lymphocyte counts.

E. C. Easson

2479. **Depth Dose of Electrons from the Betratron**
L. S. SKAGGS. *Radiology* [*Radiology*] **53**, 868–874, Dec., 1949. 3 figs., 5 refs.

2480. **Influence of Estrogens on the Acute *X*-Irradiation Syndrome**
H. M. PATT, R. L. STRAUBE, E. B. TYREE, M. N. SWIFT, and D. E. SMITH. *American Journal of Physiology* [*Amer. J. Physiol.*] **159**, 269–280, Nov., 1949. 8 figs., 8 refs.

RADIODIAGNOSIS

2481. **The Clinical Diagnosis of Bony Tumours of the Cranial Vault.** (Le diagnostic clinique des tumeurs osseuses de la voûte du crâne)
D. PETIT-DUTAILLIS and B. PERTUISET. *Presse Médicale* [*Pr. méd.*] **57**, 655–657, July 16, 1949. 14 figs., 1 ref.

The diagnosis of bony tumours of the cranial vault is difficult; in many cases histological examination is necessary for a final confirmation of the clinical diagnosis. The authors assume, however, that careful study of radiological appearances and due consideration of the clinical signs may lead to a correct diagnosis in quite a few cases. The present paper contains 14 illustrations of rather characteristic bony tumours of the cranial vault; the radiographs were chosen from the collection of the authors, from the archives of the neurosurgical clinic of Paris, and from the literature. The authors distinguish between (1) "constructive" tumours, (2) destructive tumours, and (3) diffuse tumours.

The so-called constructive tumour group is made up of osteomata and angiomata. Three different types of haemangioma can be distinguished, namely: (*a*) sun-ray haemangioma; (*b*) a bee-hive form of angioma, which may have an intracranial extension; (*c*) the so-called "grass-fire" type of haemangioma, which shows radiating bone spicules without much destruction of the outer and inner table. These constructive tumours must be carefully distinguished from: (1) bone changes produced by some infiltrating meningiomata which resemble those in Paget's disease; (2) osteoclastomata as observed in von Recklinghausen's disease; (3) false traumatic cysts of the bone; (4) calcified cephalhaematoma.

The group of destructive tumours of the cranial vault consists of osteolytic growths, which produce one or more lacunae; the diagnosis of these lesions is particularly difficult and, often enough, only possible by histological examination. The one benign tumour belonging to this group is the cholesteatoma. Malignant lesions producing a single lacuna are the osteogenic sarcoma and Ewing's sarcoma. Multiple lacunae are caused (though not invariably) by myelosarcomata and metastatic tumours; solitary secondary deposits are difficult to diagnose.

From a differential diagnostic point of view congenital or traumatic bone defects must be considered; bony lacunae caused by infective processes (tuberculosis, syphilis, osteomyelitis) are easily recognized in the presence of fistulous tracts; an exact clinical history will be of great help in these cases. Hand–Schüller–Christian's disease must also be considered; eosinophil granuloma, a special form of xanthomatosis, can be diagnosed only by histological examination. Finally Schüller's disease must be mentioned, a variety of fibrous osteitis affecting particularly the frontal, occipital, and some areas of the parietal bones.

To the group of diffuse tumours belong certain myelosarcomata and some metastatic lesions.

[The figures accompanying this paper are well chosen and deserve particular study.] *F. K. Kessel*

2482. **Bronchography with an Aqueous Contrast Medium ("Ioduron B").** (La broncografia eseguita con un mezzo di contrasto acquoso (Ioduron B))
A. GAMBIGLIANI ZOCCOLI and C. FRANZINI. *Riforma Medica* [*Rif. med.*] **63**, 1159–1161, Nov. 26, 1949. 34 figs., 4 refs.

"Ioduron" is a viscous, water-soluble, organic iodine compound. When injected into the bronchi it is rapidly absorbed, so that successive bronchographic examinations can be carried out if necessary at a few days' interval. This is not the case when iodized oils are used, for the latter leave shadows which may persist for months and which render interpretation difficult at later bronchography. *A. Orley*

2483. **Artificial Anterior Pneumomediastinum in the Analysis of Abnormal Thymus Shadows in Children.** (Le pneumomédiastin antérieur artificiel chez l'enfant. Son importance pour analyser les images anormales du thymus)
A. P. H. DEGOY and S. DI RIENZO. *Presse Médicale* [*Pr. méd.*] **57**, 1215–1217, Dec. 25, 1949. 11 figs., 17 refs.

For the radiological demonstration of the anterior mediastinum in children the authors recommend the injection of 40 to 150 cc. of air into the upper retrosternal space through the suprasternal notch. The child is screened to ascertain whether enough air has been injected and radiographs are then taken. The authors describe the appearance of the normal and pathological thymus, as demonstrated by this method, and suggest its use in myasthenia gravis, Graves's disease, Hodgkin's disease, leukaemias, status thymo-lymphaticus and status thymo-asthmaticus, infantile tetany, and pylorospasm, and for the control of dosage in radiotherapy of the thymus. *A. Orley*

2484. **Dilatation of the Jejunum**
L. E. HAWES. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **62**, 831–836, Dec., 1949. 5 figs., 15 refs.

Dilatation of the small intestine sometimes affects a single loop just above an obstruction, but it usually extends rapidly. Persistently localized dilatation is seen when the wall is involved either in an inflammatory process or in certain rapidly growing non-obstructive neoplasms. Two illustrative case histories are reported. A woman aged 61 was admitted to hospital with a story of fatigue and low fever for one month. No barium-

meal examination was carried out and no diagnosis was made. Four months later she was readmitted with the new symptoms of intermittent abdominal distension, belching, and increased flatus level. The straight film of the abdomen showed a rigid-looking loop of jejunum distended with air. A barium-meal examination was made and no mucosal pattern could be seen in the affected area. The loop was excised and the dilated piece of gut was found to be 20 cm. long by 7 cm. in diameter. The wall was about 1 cm. thick, and the luminal surface was brownish-grey and granular. A triangular wedge of whitish thickened mesentery proved on section to be due to fusion of enlarged lymph nodes. The histological diagnosis was "stem cell lymphoma differentiating into lymphoblastic lymphoma". Death from peritoneal metastases occurred 5 weeks after operation.

In the second case, which was radiologically very similar, the dilatation was due to subacute inflammation which was thought to be caused by early regional enteritis. No similar case has been found in the literature. A man aged 50 was admitted to hospital with a 5-day history of nausea and vomiting together with epigastric pain later located to the left of the umbilicus. There was some fever and leucocyte count of 12,700 per c.mm., and the clinical diagnosis was acute diverticulitis. A barium meal on the 15th day showed a dilated jejunal loop just below the duodeno-jejunal flexure. The normal mucosal pattern was replaced by a "coarsely granular or lacelike reticular pattern". The patient's condition improved and he was discharged, but 10 days later the symptoms recurred and he had to be readmitted for operation. At operation there were a number of adhesions, and a friable, soft, purplish loop of jejunum was excised. Microscopically all coats, but especially the mucosa and submucosa, were infiltrated with lymphocytes, eosinophils, and plasma cells. In the associated lymph nodes there was healed calcified lymphadenitis, probably tuberculous.

Denys Jennings

2485. **Prepyloric Local Gastritis**

J. B. HAWORTH and N. B. RAWLS. *Radiology* [*Radiology*] **53**, 720–728, Nov., 1949. 6 figs., 11 refs.

This report is based on a follow-up study of 1,289 patients, on whom the authors carried out 1,519 radiological investigations of the upper gastro-intestinal tract, It is the authors' opinion that prepyloric local gastritis is primarily a psychosomatic disorder and is most commonly found in the "nervous" type of patient. The most characteristic complaint is epigastric distress of a burning, aching, or griping character, occurring 15 to 30 minutes after food. It is frequently relieved by alkalis or demulcents and is aggravated by spices, alcohol, and coffee. Haemorrhage was reported in 12% of the authors' cases of uncomplicated prepyloric local gastritis. Because of the rarity of surgical intervention, sufficient material for histological examination was obtained in only 9 cases, in which lymphocytic infiltration and thickening of the gastric mucosa was found, often associated with oedema of the submucosal connective tissue.

The radiological diagnosis is based on the following criteria: (1) The presence of an initial gastric fluid residue. (2) Visible prepyloric mucosal deformity, characterized by thickening of the individual folds and varying degrees of distortion of pattern. (3) Localized prepyloric tenderness on deep pressure. (4) Spasm along the distal portion of the lesser curvature, with or without pylorospasm. (5) Interference with normal peristalsis and "antral systole". The presence of any four of these criteria is sufficient for diagnosis, provided mucosal deformity and local tenderness are amongst them. Treatment with a bland diet and aluminium hydroxide gel as for a peptic ulcer is recommended, the patient being urged to discontinue the use of alcohol, tobacco, and coffee. Atropine or belladonna is given by the authors in moderate dosage, with phenobarbitone where it seems desirable. "Pyribenzamine", 50 mg. 4 times a day, is given for the first 2 weeks, after which the dose is adjusted according to the indications in the individual case, administration being continued for some 6 months.

Out of the 1,289 cases investigated, prepyloric local gastritis was found in 109 (8·5%) and was associated with other gastro-duodenal abnormalities in a further 176 (13·7%). The condition was found slightly less frequently than duodenal ulcer, but more than twice as frequently as gastric ulcer. There was no significant difference in incidence between the two sexes.

L. G. Blair

2486. **Radiological Differential Diagnosis of Gastric Polyposis.** (Beitrag zur röntgenologischen Differentialdiagnostik der Polyposis ventriculi)

R. ALTMANN. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **71**, 896–900, Oct., 1949. 2 figs., 11 refs.

Typical radiographs of multiple gastric polypi are reproduced. Gastroscopy in this case merely revealed a combination of atrophic and mild hyperplastic gastritis. Clinically, upper abdominal discomfort, loss of appetite, and loss of weight suggested carcinoma and there was achlorhydria after histamine injection. The case was re-studied by radiography and gastroscopy, and it was concluded that irregular contractions of the muscularis mucosae must be responsible for the symptoms. It is stated that no reports of similar cases could be found in the literature.

[Cases of this kind are probably not so very rare. There is no risk of a mistake if gastroscopy is always insisted upon.] *Denys Jennings*

2487. **The Radiology of Intermittent Gastric Volvulus in Infants.** (Il quadro radiologico del volvolo gastrico intermittente nel lattante)

R. DELLA CASA. *Archivio Italiano di Pediatria e Puericoltura* [*Arch. ital. Pediat.*] **13**, 217–234, 1949. 23 figs., 7 refs.

Intermittent gastric volvulus is not uncommon in the first year of life. Radiographic investigation is indicated in cases of persistent vomiting in young infants, particularly when the stools appear normal. The author

describes 7 cases, in 6 of which vomiting occurred frequently. In 2 of these cases repeated radiological examination led to a diagnosis of gastric volvulus, and in the others the radiological picture showed a similar stomach deformity, though repeated examination was not possible. *A. Orley*

2488. **Lipomas of the Gastrointestinal Tract**
W. L. PALAZZO. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **62**, 823–830, Dec., 1949. 7 figs., 15 refs.

Only 36 cases of lipoma of the gastro-intestinal tract have been found in the files of the Massachusetts General Hospital since 1900. Of these, 22 occurred in 12,100 necropsies. (This compares with Schottenfeld's figure of 46 in a collected series of 37,741 necropsies from various sources.) [The age and sex incidence of the whole necropsy series is not given, but if it corresponds with that of most general hospitals there is no evidence that either sex is more liable to lipomata or that the incidence increases markedly with age.] Of the 13 lipomata which caused symptoms 7 were pedunculated, 9 were ulcerated, and all except 3 were over 3 cm. in diameter; 2 were in the ileum and 11 in the colon. Of the 23 in the asymptomatic group 17 were sessile, none was ulcerated, and all except one were under 3 cm. in diameter; 6 were in the stomach, 8 in the small intestine, and 9 in the colon.

The symptoms, when there were any, were those of intermittent obstruction or intussusception; in a few patients bleeding per rectum took place. The length of history ranged from 4 days to 10 years. The radiological findings were those of obstruction, intussusception, a polyp, or an intramural tumour. The diagnosis from a spindle-cell tumour or a polypoid cancer is usually impossible. *Denys Jennings*

2489. **Evaluation of Tomography as a Possible Means of Radiological Study of the Bladder.** (In merito alle possibilità di impiego della stratigrafia nello studio radiologico della vescica urinaria)
A. GRILLI and G. C. VERDECCHIA. *Radiologia* [*Radiologia, Roma*] **5**, 381–388, Oct.–Dec., 1949. 8 figs., 2 refs.

The authors recommend tomography in the examination of the urinary bladder. They prefer air as the best contrast medium for outlining the bladder, and claim that tomograms of the air-filled bladder give the maximum amount of information about deformities of the walls of the bladder, particularly in cases of tumour.
A. Orley

2490. **Tomography in Combination with Pneumoperitoneum as a New Means of Studying Intra- and Extraperitoneal Organs.** (Nuove possibilità di studio dei visceri intra ed extraperitoneali con l'associazione stratigrafia-pneumoperitoneo)
A. GRILLI. *Radiologia* [*Radiologia, Roma*] **5**, 337–344, Oct.–Dec., 1949. 10 figs.

The author suggests a combination of pneumoperitoneum with tomography for the investigation of intra- and retroperitoneal viscera. Radiographs taken by this method (of which a number are reproduced) plainly show deformities and displacement of viscera which are difficult to demonstrate by ordinary radiography or with pneumoperitoneum alone
A. Orley

2491. **Tomography in Tuberculous Spondylitis.** (Beitrag zur Tomographie der Spondylitis tuberculosa)
E. SOMMER. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **6**, 189–201, 1949. 9 figs., 13 refs.

Early diagnosis of tuberculous spondylitis can be made and the course of the disease more easily judged by tomography of the spinal column. This method was used in the examination of cases of spondylitis at the Braunwald Sanatorium. Three illustrative cases are discussed. Lesions are seen earlier in the tomograph and appear larger than when ordinary radiographs are taken. *W. J. Czyzewski*

2492. **The *X*-Ray Picture of Osteoporosis in the Theresienstadt Concentration Camp.** (Das Röntgenbild der Osteoporose im Konzentrationslager Theresienstadt)
L. POKORNÄ. *Radiologia Clinica* [*Radiol. clin. Basel*] **18**, 360–370, Nov., 1949. 5 figs.

Cases of osteoporosis observed among the inmates of a concentration camp showed changes in bone structure as well as in the shape of the bones. The structural changes took the form of rarefaction, while the changes in shape varied according to the bones involved. The thorax was almost always bell-shaped, mostly symmetrically, but in one case unilaterally deformed. Pelvic changes consisted of bone flattening and marked narrowing of the true conjugate diameter. The picture of insidious fracture in osteoporosis of the pubic bones is described and the resemblance to the mechanism of necrosis of the os lunatum is pointed out. The changes in the spine consist of flattening, the vertebrae sometimes assuming a wedge shape. *A. Orley*

2493. **Herniated Disks and Vertebral Ligaments on Native Roentgenograms.** [In English]
Á. KOVÁCS. *Acta Radiologica* [*Acta radiol., Stockh.*] **32**, 287–303, 1949. 18 figs., 22 refs.

In the diagnosis of suspected lesions of the intervertebral disks, evidence obtained from a " native " (that is, a conventional) radiograph, may make the injection of opaque material into the spinal canal superfluous. The author, writing from the St. John Hospital, Budapest, claims that this is so in 80% of cases. The principal indirect signs pointing to herniation of an intervertebral disk are narrowing of the disk space and malalignment of the vertebral margins, especially if this malalignment is variable and alters with flexion and extension of the spine. In this respect emphasis is placed upon the posterior vertebral border. Positive and direct evidence of disk displacement is obtained when there is sufficient calcium salt present in the disk to render this directly visible. The importance of careful positioning is emphasized, since an erroneous impression of malalignment is sometimes obtained when the spine is slightly rotated. Of the author's 99 cases in which disk hernia-

tion was diagnosed on the plain *x*-ray findings, the lumbo-sacral disk was involved in 68; for this reason the author advocates that, in addition to the routine antero-posterior and lateral views, his oblique "lumbo-inguinal" view should be taken. In this projection, views are taken through the lumbo-sacral foramen on each side. This provides a tangential view of the lateral portions of the posterior disk surfaces, and a number of radiographs are reproduced in which the actual disk protrusion can be seen. Trauma to the posterior longitudinal ligament, caused by herniation of the disk, and also inflammatory changes in the ligaments, give rise to the deposition of calcium and result in linear, arc-like shadows which embrace the intervertebral space posteriorly. If this shadow is incomplete it may be visible as a hook-like osteophyte encroaching upon the neural foramen and probably giving rise by direct irritation to symptoms of sciatica. *A. M. Rackow*

2494. **The Radiological Localisation of the Placental Site. Part II.—The Radiological Diagnosis of Placenta Praevia**

F. Reid. *British Journal of Radiology* [*Brit. J. Radiol.*] **22**, 643–665, Nov., 1949. 22 figs., 25 refs.

The author applies the following basic principles to distinguish between a normal and a low implantation of the placenta. (1) In vertex presentations before engagement the foetal head normally rests symmetrically on the pelvic brim when the mother is standing upright. (2) The junction of the upper and lower segments is usually in the neighbourhood of the pelvic inlet during the last 2 or 3 months of pregnancy. (3) If implantation extends on to the lower segment the foetal head will be displaced by the placenta from its normal position at the brim.

Provided the bladder and rectum are not distended, radiographs taken with the patient erect or semi-erect show the minimum distance from the head to both pubes and promontory. During the last 2 months of pregnancy this gap is rarely larger than 1·2 cm. when it is occupied by the uterine wall only. If a placenta praevia intervenes the presenting part will be displaced either upwards and backwards from the pubes, or forwards from the promontory, or upwards from both the pubes and the promontory.

Apparent displacement may be caused by: (1) laxity of the abdominal muscles; (2) smallness of the presenting part in relation to the conjugate diameter of the pelvic inlet; (3) steep inclination of the brim. As a general rule the author considers that implantation has taken place on the lower segment only if the presenting part is over 2 cm. from either the pubes or the promontory.

For patients not allowed to stand, the following arrangement was found to be of value: The mother lay supine on a tilting table and the head end was raised 50 or 60 degrees. The following films were then taken: (*a*) antero-posterior view of the abdomen, including the pelvic inlet; (*b*) a lateral view of the pelvis; (*c*) a lateral view of the abdomen. If the patient was allowed to stand the lateral views were taken with her in the erect position. If the gap between presenting part and promontory was found to exceed 2 cm. then a lateral radiograph of the pelvis was taken with the patient lying supine on the table, to differentiate between true and apparent displacement. Forward displacement of the presenting part simulating a low implantation may be due to an accumulation of faeces in the pelvis. Similarly, backward displacement may be caused by a full bladder.

The author analysed 372 cases at the Radcliffe Infirmary and found a normal implantation in 299 of them. Radiographs suggested a low implantation in 73 cases. Of the latter the diagnosis was clinically verified in 31 cases. The 299 radiologically normal cases did not present any clinical difficulty. The accuracy of this method depends upon using the foetus as a contrast medium to locate the lining of the lower uterine cavity. If, however, the presenting part is the breech instead of the cranium, the task is much more difficult because of the irregular shape of the breech and the frequent non-visualization of its outline, which is often obscured by the dense bones of the maternal pelvis. With a transverse lie the difficulties found in breech presentation are considerably accentuated. *J. Rabinowitch*

2495. **Studies on Hysterosalpingography. Comparison of the Value of Water-soluble and Oil-soluble Contrast Media.** (Recherches sur l'hystéro-salpingographie. Valeurs comparées des milieux de contraste oléo-solubles et hydro-solubles: méthode de Kjellberg)

J. Varangot and M. Bommelaer. *Gynécologie et Obstétrique* [*Gynéc. et Obstét.*] **48**, 437–464, 1949. 37 figs., 14 refs.

This study is described as one of comparison between oil- and water-soluble media in hysterosalpingography, but it is more than that, since it describes an extension of the technique commonly used for determination of tubal patency to the investigation of a variety of pathological conditions in the pelvis.

The authors give a brief history of the development of the technique of salpingography, and discuss the relative advantages of oil- and water-soluble media. They note that a 6-cm. layer of iodized oil containing 40% iodine is sufficient to obscure any underlying image inside, or adjacent to, the uterus. They reproduce some convincing radiographs of objects contained in a rubber balloon, which are clearly visible in the water-soluble medium, but not in the oil. They agree with Montgomery that "the ideal medium should give adequate radio-opacity, be rapidly absorbed, completely harmless, non-irritant, and have an adjustable viscosity which can be altered at will".

They regard a 3% solution of polyvinylpyrrolidone, introduced in March, 1940, as coming nearest to satisfying these requirements.

The technique of Kjellberg is described; he used it not only to outline the tubes, but as a general diagnostic procedure for all kinds of abdominal conditions. He used 40 to 60 ml. of fluid and took as many as 14 films. This technique is too expensive and time-consuming, and the authors have reduced the number of films to 6. The paper is illustrated by many radiographs showing such varied conditions as fibroids, polypi, and endometriosis which may be accurately diagnosed by this method.

They give the constitution of the many products now marketed, together with the *p*H, and show that all are

hypertonic and therefore do cause some pain. They use a 2% mixture of local analgesic with diodone (more recently they have added penicillin) and find that this permits a satisfactory painless examination of the whole of the pelvic cavity. They have encountered allergic reactions in 1 in 1,000 cases. They use aminophylline as an antispasmodic. The infection rate is 1 in 200; it is emphasized that this technique is not just an improvement of the " lipiodol " method but is an entirely different method of diagnosis.

They conclude by giving a table of average measurements as follows, based on 300 cases examined.

I. Uterine cavity with tubal insufflation.
  (*a*) Infantile uterus, 3 ml.
  (*b*) Normal uterus, 5 ml.
  (*c*) Fibroid uterus, from 7 to 25 ml.

II. Uterine injection and obstructed tubes (the quantity necessary for uterine injection only in a normal uterus is about 4 to 7 ml.).
  (*a*) Uterus and 2 normal tubes obstructed at the ampulla, 11 ml.
  (*b*) Uterus and tubes showing some dilatation of the ampulla, 15 ml.
  (*c*) Uterus and unilateral hydrosalpinx, up to 25 ml.
  (*d*) Uterus and bilateral hydrosalpinx, up to 35 ml.

III. For pelvigraphy, from 30 to 60 ml. of mixture as required.

In 50% of the cases passage of the fluid was painless, and in 90% of the cases all fluid had disappeared from the peritoneal cavity in less than 6 hours.

[This article is extremely competently written and is profusely illustrated. The original should be consulted.]

B. Sandler

2496. **The Absorption of Radiopaque Substances Used in Hysterosalpingography. A Comparative Study of Various Aqueous and Oily Media**

W. E. Brown, A. F. Jennings, and J. T. Bradbury. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **58**, 1041–1053, Dec., 1949. 9 figs., 17 refs.

The authors carried out hysterosalpingography in 200 cases and in this paper report on the comparative findings in 118 of these in which the hysterosalpingography was performed with one of the following five radio-opaque media: " rayopake ", " skiodan ", " lipiodol ", " iodochlorol ", and " lipoiodine ". Each of these substances was tested for absorption time, viscosity, radio-opacity, and clinical reactions, and 38 patients were examined at subsequent laparotomy for tissue reaction and the presence of retention cysts. The authors find that iodized oils (especially " lipiodol ") give dense radiographic shadows and that the long period of absorption, which frequently exceeds 6 months, permits of the taking of radiographs hours or days after the injection of the dye for demonstration of tubal patency. The disadvantages include the possibility of retention-cyst formation for many months or even years, retention of oil in the pelvic cavity for a considerable time, and a transient peritoneal reaction with pain, fever, and a leucocytosis. Oil embolism has been known to occur, but was not seen in the present series. With aqueous media the genital tract was satisfactorily visualized without the hazards of retention-cyst formation and pulmonary embolism. Absorption from the tubes and peritoneal cavity is extremely rapid and an alteration in the customary technique of exposure is therefore required. It is essential that the injection be carried out on the *x*-ray table and that films be taken during the introduction of the dye and immediately afterwards, for frequently the whole medium has vanished from the genital tract within 25 minutes. The low viscosity of skiodan results in too rapid peritoneal spill with consequent overshadowing of the tubal outlines. The authors consider rayopake to be the medium of choice because of its rapid absorption and the relative freedom from the many untoward reactions encountered with oily media.

[The abstracter has not found it satisfactory to take films alone when an aqueous medium is being used. It is often not possible to outline the tubes, as either all the dye has already spilled into the peritoneal cavity or, when the tubes are blocked, it has flowed back into the uterus and vagina as soon as the nozzle is removed from the cervical os. It has therefore been his custom to carry out all these examinations under screening control. The advantage is the immediate visualization of a point of blockage or a hydrosalpinx, and overfilling with a possible rupture of a tube is thus prevented. A spill-over can be seen as soon as it occurs and the minimum of medium is used for the examination, thus greatly decreasing the amount of peritoneal discomfort normally associated with peritoneal spill. It is also possible to prevent the pain of uterine distension by watching the degree of stretching which the uterus undergoes on introduction of the medium and to alter the rate of injection accordingly. Another advantage is that it is no longer necessary to take films blindly in the hope that they will show the desired feature, since it is possible to determine accurately the most opportune moment for the exposure. Sometimes it may not be necessary to take a film at all.]

J. Rabinowitch

2497. **Angiocardiography and Aortography in the Diagnosis of Congenital Cardiovascular Lesions**

T. H. Burford, M. J. Carson, and W. G. Scott. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **18**, 860–868, Dec., 1949. 11 figs., 13 refs.

2498. **The Role of Angiocardiography and Venography in Mediastinal and Paramediastinal Lesions**

O. A. Abbott, W. A. Hopkins, and T. F. Leigh. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **18**, 869–898, Dec., 1949. 19 figs., 12 refs.

2499. **Electrokymography of the Heart and Great Vessels: Principles and Application**

B. R. Boone, G. F. Ellinger, and F. G. Gillick. *Annals of Internal Medicine* [*Ann. intern. Med.*] **31**, 1030–1056, Dec., 1949. 16 figs., 34 refs.

2500. **Bronchographic Aspects of Certain Pulmonary Regions.** (Aspects bronchographiques de quelques territoires pulmonaires)

J. Ioannou. *Presse Médicale* [*Pr. méd.*] **57**, 1208–1209, Dec. 25, 1949. 16 figs., 3 refs.

Pathology

2501. **The Origin of Melanotic Tumours.** (Zur Entstehung der melanotischen Tumoren)
B. DAVIDS. *Archiv für Ophthalmologie* [*v. Graefes Arch. Ophthal.*] **149**, 449–459, 1949. 32 refs.

His own histological studies, together with the more recent literature on the formation and the biological role of melanotic pigments, have led the author to a reconsideration of the possible causative importance of the pigment. Melanin is said to be a product of the nucleolar substances of the cell nucleus which can diffuse into the plasma. Precursors of melanin have been labelled by certain investigators as "virulent nucleoproteins" possessing a "virus-like" capacity of auto-catalytic reduplication. Investigations into the mechanism of the dihydroxyphenylalanine (DOPA) reaction have shown that if tyramine is treated with extracts of adrenal cortex, adrenaline-like substances result; intermediate products of this reaction, hydroxytyramine and epinin, can produce melanin with the help of cutaneous ferments. Melanin itself has been claimed to have a vasoconstrictor and hypertensive effect. The argument is that, far from being a simple by-product of the tumour, melanin may in itself be the causative agent of melanotic growth. The special importance of this hypothesis lies in the fact that it postulates an autosomatic factor as an agent of malignant growth. A cancerogenetic action of adrenaline is considered improbable.

[Though highly speculative, this is a stimulating article.] *P. L. Kiewe*

2502. **The Determination of the Level of Leukocytes in the Blood Stream with Inflammation. A Thermostable Component Concerned in the Mechanism of Leukocytosis**
V. MENKIN. *Blood* [*Blood*] **4**, 1323–1337, Dec., 1949. 4 figs., 18 refs.

There is present in inflammatory exudates, particularly in exudates having an acid hydrogen ion concentration, a thermostable leukocytosis-promoting component, which in conjunction with the previously described thermolabile leukocytosis-promoting factor aids in our understanding of the mechanism of leukocytosis with many inflammatory states. The thermostable component of the leukocytosis-promoting factor is recovered in association with the pyrogenic factor or pyrexin. Whether it is essentially different chemically from the active principle present in the thermolabile factor is discussed and remains to be seen.

The resultant leukocyte level in the blood stream with a concomitant inflammation is the resultant of a multiplicity of factors. The rise in the number of circulating leukocytes with inflammation is induced by a combination of the thermolabile and the thermostable components of the leukocytosis-promoting factor of exudates; whereas the decrease in white blood count seems referable to both leukopenin and the leukopenic factor of inflammatory exudates. A predominance in the concentration of any one of these factors liberated by injured cells at the site of an acute inflammation will determine the final level of white cells in the circulation.—[Author's summary.]

EXPERIMENTAL PATHOLOGY

2503. **Liver Damage Produced by Feeding Alcohol or Sugar and its Prevention by Choline**
C. H. BEST, W. S. HARTROFT, C. C. LUCAS, and J. H. RIDOUT. *British Medical Journal* [*Brit. med. J.*] **2**, 1001–1006, Nov. 5, 1949. 6 figs., 22 refs.

Ashworth (*Proc. Soc. exp. Biol., N.Y.*, 1947, **66**, 382) concluded from experiments on "pair-fed" rats that alcohol exerted a toxic effect on the liver even when the diet was adequate. In the present paper the authors point out that in Ashworth's experiments the calorie intake of the animals consuming alcohol was considerably greater than that of those drinking water only. Further experiments are described in which the growth curves and liver changes in groups of white rats consuming alcohol were compared with those in animals given a diet of the same calorie value, but not receiving alcohol, the extra calories in the latter group being supplied as powdered sucrose (0·15 g. for each 1 ml. alcohol). The alcohol used in these experiments was a 15% watery solution of purified distilled ethyl alcohol and basic diet was designed to be "as nearly adequate as possible in all its components except the lipotropic factors". The choline content of the diet was designed to maintain the total lipid content at about 10% of fresh liver weight. The effects of lipotropic supplements (methionine, choline chloride, or casein) to the diets of certain groups of rats was also studied. The average total lipid content and incidence of fibrosis in the liver in the various groups of animals were determined after 6 months.

No abnormalities were detected in the livers of animals given diets with lipotropic supplements, whether alcohol was taken or not. All the rats consuming alcohol and not receiving lipotropic supplements developed fatty livers (average total lipid content 18%) and 7 out of 15 of them some hepatic fibrosis. Similarly, all those receiving sugar in place of alcohol, but otherwise taking a diet identical with the alcohol-fed rats, had a high liver lipid content (average 26%) and 7 out of 9 developed fibrotic changes. The rats given the basic diet *ad lib* gained on the average 262 g. over the full period of the experiment (about 180 days). Those given the basic diet *ad lib.* with alcohol gained 182 g., their daily food intake being less than the first group by about 3 g. per day and their caloric intake, after allowing for the alcohol consumed, also being less. The rats fed isocalorically, but receiving sucrose instead of alcohol

(0·15 g. for each 1 ml. alcohol), gained slightly more weight than those receiving alcohol. The authors consider that this stunting effect in the alcoholic animals was due to the diminished food intake and not to any specific effect of the alcohol " unless one is willing to make the highly improbable assumption that sucrose exerts the same toxic effect as alcohol ".

These experiments show that, in white rats, long-continued consumption of purified ethyl alcohol can cause accumulation of fat in the liver and subsequent hepatic fibrosis if the animals are fed on a diet lacking adequate amounts of lipotropic factors. However, isocaloric feeding with sucrose in place of alcohol causes similar lesions, and since they could be prevented in both groups by supplementing the diet with choline the authors conclude that " the idea of a specific toxic effect of alcohol upon the liver cells receives no support ". They suggest that " an imbalance between calorie intake and supply of accessory food factors is the cause of the liver lesions: the extra calorie intake induces a specific deficiency when the basal diet is marginal with respect to any one vitamin. Both alcohol and sugar, when taken in excess, supplant choline-containing foodstuffs and at the same time, by increasing the calorie intake, augment the demand for the lipotropic agents ". The possible relation of these experimental results to alcoholism in the human subject is discussed. *B. G. Maegraith*

2504. **Degenerative Renal Lesions Induced By Prolonged Choline Deficiency**

J. J. LALICH, B. E. KLINE, and H. P. RUSCH. *Archives of Pathology* [*Arch. Path.*] **48**, 583–592, Dec., 1949. 8 figs., 8 refs.

The authors describe changes in the renal parenchyma in batches of hooded and Sprague-Dawley rats subjected to choline deficiency for many months.

Two-thirds of each batch of rats were fed on a low-choline diet similar to that described by Copeland and Salmon (*Amer. J. Path.*, 1946, **22**, 1059) and the remainder on the same diet with 2 g. choline added per kg. Rats on the choline-deficient diet were given choline by stomach-tube for the first fortnight of the experiment. Fifteen controls and 23 test rats were examined after 6 to 19 months. The results are detailed in the present paper.

Pathological lesions appeared in the liver, kidneys, and lungs of the choline-deficient animals. The liver showed fatty changes and cirrhosis. " The majority of the rats in the control and deficient groups had purulent bronchitis and terminal broncho-pneumonia ". In the choline-deficient groups there was progressive increase in size of the kidneys, depending on the severity of the lesions.

The commonest early change in the kidneys was the presence of eosinophilic or slightly basophilic homogeneous casts, occasionally with desquamated epithelial cells. Initially these appeared in the distal convoluted tubules; they later became larger and were associated with " distinct tubular dilatation ". The epithelial cells of dilated tubules were flattened, atrophic, or absent. At first these lesions appeared in segments, later more generally, with reduction in the number of tubular elements, and increased peritubular connective tissue and cellular foci. The glomerular tufts were shrunken and Bowman's space was dilated and filled with eosinophilic material. In the areas most affected there were extensive interstitial fibrosis and hyalinization of the glomeruli. Normal tubules and glomeruli were present in adjoining areas. Focal arteriolar changes (hyalinization and hypertrophy) were present in half the choline-deficient rats. " Significant interstitial fibrosis occurred only in the deficient rats; it was not observed in the control group ". Intratubular calcification occurred in the cortico-medullary area in 90% of all animals. The incidence of the renal lesions was greater in the test animals, but there were extensive changes in some of the controls. For example, tubular involvement without glomerular destruction occurred in 3 out of 8 control Sprague-Dawley rats.

The authors review the literature on renal changes developing in choline deficiency. They suggest the following sequence of events: vacuolation of the epithelial cells of the proximal convoluted tubules; eosinophilic or basophilic casts in the distal tubules and Henle's loops; obstruction of the proximal segments with tubular dilatation; collection of protein material in Bowman's space, dilating the capsule and compressing the tuft; fibrosis and atrophy of the glomeruli; focal hyalinization and hypertrophy of arterioles. They consider that their observations have little direct bearing on the pathology of human renal disease.

[The pathogenesis of the initial lesions in the tubules is not discussed, although reference is made to Hartcroft's suggestion that cortical capillary ischaemia may develop (*Brit. med. J.*, 1949, **1**, 424).] *B. G. Maegraith*

2505. **Isolation of Mouse Mammary Carcinoma Virus**

S. GRAFF, D. H. MOORE, W. M. STANLEY, H. T. RANDALL, and C. D. HAAGENSEN. *Cancer* [*Cancer*] **2**, 755–762, Sept., 1949. 5 figs., 9 refs.

The authors claim to have isolated characteristic virus-like particles, of a size ranging from 50 to 130 mμ, from the milk of Paris R III high-breast-cancer-strain mice. Similar particles could not normally be found in the milk of C57 low-breast-cancer-strain mice, but were isolated from the milk of mice of that strain which had been foster-nursed by R III females. These particles were found after coagulation of the casein or hydrolysis of the proteins of the R III-strain milk by crystalline chymotrypsin or by decalcification of the milk, followed by two cycles of differential high-speed centrifugation, each at 40,000 revolutions per minute (r.p.m.) for 30 minutes. The deposit obtained from this centrifugation was examined by means of the electron microscope and found to contain the characteristic spherical particles. It was shown on injection into 10-to-14-day-old C57 mice to induce mammary carcinoma in over 40% of the animals.

[No reference is made to experimental results published by Passey, Dmochowski, Astbury, Reed, and Johnson (*Nature, Lond.*, 1947, **160**, 565; and 1948, **161**, 759). In these two papers the finding is reported of spherical particles, mostly about 20 to 30 mμ in size, in extracts of normal and malignant tissues, and in the milk, of mice

from several high-breast-cancer strains, and their absence or extreme scarcity in similarly prepared extracts and milk from low-cancer-strain mice. The present authors report biological tests on the deposits after two centrifugation runs at 40,000 r.p.m. No mention is made, however, of biological tests of the corresponding supernatants. This is an important point which has to be borne in mind when drawing final conclusions about the possible relationship between their particles and the Bittner factor. Nor is mention made of electron-microscope examination of the supernatants. They do, however, report the results of biological tests of supernatants and sediments obtained after centrifugation at the same speed of untreated R III-strain milk, in which hardly any difference in tumour-inducing activity was found between the supernatants and the sediments. Passey *et al.* (*Nature, Lond.*, 1950, **165**, 107) reported that after centrifugation at the same speed for 2 hours the supernatants, as observed under the electron microscope, were apparently free from particles, whereas after 1 hour's centrifugation they still contained a number of the characteristic particles. Both the supernatants and the sediments were tested biologically, and so far no tumours have developed in mice injected with the supernatants apparently free from particles, while the sediments and the supernatants with particles have given rise to tumours in test mice. The difference between the range of size of the particles as reported in the present paper and as reported by Passey *et al.* may be the result of the different treatment applied which, however, has not destroyed the tumour-inducing activity in either case. At present, evidence is accumulating that what appear to be larger particles are in many cases, if not always, aggregates (and often symmetrical aggregates) of smaller units.] *L. Dmochowski*

2506. **Factors Affecting the Distribution of Tumor Metastases; Experiments with V_2 Carcinoma of Rabbits**
D. R. COMAN, R. B. EISENBERG, and M. MCCUTCHEON. *Cancer Research* [*Cancer Res.*] **9**, 649–651, Nov., 1949. 5 figs., 2 refs.

In order to study the factors determining the anatomical distribution of tumour metastases, a saline suspension of cells of the transplantable squamous carcinoma V_2 derived from the Shope rabbit papilloma was injected intravascularly into rabbits. This type of tumour, when transplanted, spreads regularly to adjacent lymph nodes and occasionally to the lungs, but rarely elsewhere. Injection of the suspension into the femoral artery of 8 animals resulted in extensive tumour infiltration of the leg muscles in all cases: there was no indication that muscle provided an unfavourable "soil" for tumour growth. Injection into the left side of the heart of 6 rabbits resulted in tumour growth in skeletal muscles in all 6, the myocardium in 5, and the lungs in 5, the less frequent sites being kidneys (4), anterior chamber of the eye (3), liver (2), pancreas (2), and adrenals, bowel, brain, lymph nodes, and spleen (one each). When heavy suspensions were injected into the femoral vein or the right side of the heart, innumerable tumour nodules developed in the lungs, but none elsewhere. Evidently the cells were unable to pass through the lungs. Under the conditions of the experiment no organ appeared to provide unfavourable "soil" for tumour growth and the authors believe that scarcity of metastases in an organ is attributable to scarcity of tumour cells reaching that organ.

[The relevance of these experiments to natural metastases is doubtful in the absence of evidence that the suspensions contained fragments similar in size to those which ordinarily are liberated into the blood stream from primary tumours.] *L. Foulds*

2507. **Experimental Study of the Anatomical and Physiological Effects of Ultraviolet Irradiation.** (Contribution expérimentale à l'étude des modifications anatomo-physiologiques provoquées par irradiation ultraviolette)
R. VERMEERSCH.. *Acta Physiotherapica et Rheumatologica* [*Acta physiother. rheum. belg.*] **4**, 261–276, Sept.–Oct., 1949. 5 figs., 32 refs.

After a brief review of the literature [from which any reference to the work of Findlay (*Lancet*, 1928, **2**, 1070 and *ibid*, 1930; **1**, 1229) is omitted], experiments are described in which albino mice were irradiated with ultraviolet light in order to induce tumours of the skin. The source of light was a 120-watt mercury vapour lamp from which the glass screen had been removed, placed 40 cm. above the cage. The wave-length of radiation was 6,000 to 2,000 Å. Albino mice of a single strain known to be free from spontaneous tumours of the skin were employed, 25 being used for each of 3 experiments.

In order to secure an intense homogeneous irradiation, the animals were kept moving in perforated metal cylindrical cages. The dosage of radiation given increased progressively to respective maxima of 30 minutes on alternate days, 1 hour each day, and 5 hours each day.

In the first weeks of irradiation many animals died in collapse. The survivors developed erythema of the ears and tail, followed by fibrosis which occasionally proceeded to sarcoma, hyperkeratosis, and finally papilloma and carcinoma formation. The maximum total yield of tumours in any one group was 75·2%, and the latent period 3 to 4 months for papillomata and 7 to 8 months for carcinomata. The ears were particularly liable to be affected. There was an associated oedema and subsequent opacity of the cornea, thought to be due to lack of vitamin A and somewhat ameliorated by administration of that substance.

The general reactions, such as collapse, paralyses, and diarrhoea were also studied. Submucous haemorrhages were found post mortem in the intestine, and there was a general loss of weight. *G. M. Bonser*

2508. **Effect of 20-Methylcholanthrene on the Transplantability of Skin of Mice**
M. SILBERBERG, R. SILBERBERG, and B. HULBERT. *Archives of Pathology* [*Arch. Path.*] **45**, 722–741, June, 1948. 7 figs., 3 refs.

In 170 mice of the RF (i) strain, 4 to 6 months old, 228 auto- and 112 homo-transplants were carried out. Both types of transplants were made with normal skin and with skin which had been painted for 2 to 12 weeks with 20-methylcholanthrene, while the skin of the

recipient area was in some cases normal and in others had been similarly treated with the carcinogen for varying periods.

The percentage of surviving homo-transplants was lower, and their survival time shorter, than those of the corresponding auto-transplants, and in no case was the surface epithelium of the transplants seen to join the margin of the wound. Auto-transplants of normal skin into wounds made in the painted skin were successful in only 10% of cases, largely as a result of changes in the wound caused by the carcinogen, the percentage success when the recipient area was normal being 68. Auto-transplants of painted skin, whether into normal or painted skin, were never seen to unite with the epithelium of the wound, the reasons being lack of epithelial outgrowth of the grafts and oedema of the wound caused by the carcinogen. The authors conclude that application of this carcinogen has the effect of decreasing, rather than increasing, the transplantability of the skin of mice. *L. Dmochowski*

2509. **Excretion and Reabsorption of Sodium and Water in the Adrenalectomized Dog**
J. C. Roemmelt, O. W. Sartorius, and R. F. Pitts. *American Journal of Physiology* [*Amer. J. Physiol.*] **159**, 124–136, Oct., 1949. 2 figs., 29 refs.

See also Section Pharmacology and Therapeutics, Abstracts 2421–6.

2510. **The Significance of Functional Differentiation in Mammary Tumours**
B. D. Pullinger. *Lancet* [*Lancet*] **2**, 823–828, Nov. 5, 1949. 5 figs., 15 refs.

In a first series of experiments, carried out to assess the effect of the administration of oestrone on the behaviour of the mammary glands in mice spayed at puberty, a quantitative relation between the degree of acinar differentiation and amount of secretion to the dose of oestrone was observed. A second series of experiments was undertaken to elucidate the factors responsible for the known tendency of spontaneous mammary tumours of mice to differentiate into acini and produce secretion, the results of which, together with the former observation, form the basis of a hypothesis that this tendency is most probably due to oestrone elaborated within the tumour cells themselves.

This hypothesis is examined in the light of what is alteady known about mammary tumours in mice and about tumours in general. The view is put forward that in breast tumours of mice which possess the Bittner factor the tumour cells, under the influence of this factor, elaborate an oestrogen-like substance, whereas in breast tumours of mice without the Bittner factor a chemical change within the tumour cells leads to the production of a similar oestrogenic stimulus. In both types of breast tumour this stimulus is responsible for the division, differentiation, and secretion of the tumour cells. Similarly, in tumours of the prostate gland an androgen-like substance may provide the stimulus for the division of the tumour cells. A plan of experimental approach towards this hypothesis is presented, and the difficulties entailed in a search for intracellular stimuli in tumour cells are discussed. *L. Dmochowski*

MORBID ANATOMY

2511. **Embolization with Material From Atheromata**
F. G. Zak and K. Elias. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **218**, 510–515, Nov., 1949. 7 figs., 14 refs.

The authors describe 3 cases of atheromatous embolism. In the first case dissemination of atheromatous material from the ulcerated aorta to various abdominal organs and to the bone marrow, periosteum, and thyroid had taken place some years previously. Microscopically, the vessels of these organs were plugged by amorphous material which incorporated cholesterol crystals. Around these there was frequently a foreign-body giant-cell reaction. The second case represented the acute phase, in which a coronary atheromatous plaque had ruptured as a result of haemorrhage into it and had produced at the periphery of the infarcted area the picture of a periarteritis, the inflammatory exudate including many eosinophil leucocytes, while the occluded arteries were plugged by material similar in appearance to that found in the first case. Small areas of myocardial scarring were noticed in the vicinity. In the third patient occlusion of a large branch of a renal artery by material from an atheromatous mitral valve had produced renal scars, and emboli had also lodged in arteries of the pancreas and spleen. This amorphous material was lying embedded within the arterial wall and had been overgrown by a layer of intima. The authors suggest that atheromatous embolism occurs more frequently than has been thought hitherto. *R. Salm*

2512. **The Myth of Chromophobe Adenomas.** (Myten om de kromofoba hypofysadenomen)
H. N. Antoni. *Nordisk Medicin* [*Nord. Med.*] **43**, 6–10, Jan. 6, 1950. 4 figs., 2 refs.

In this short but most interesting paper, the author reports that histological examination of 10 so-called chromophobe pituitary adenomata showed that 8 of them were actually gliomata (in the terminology of Cushing and Bailey, ependymomata). Of these 8 patients 2 had died and the whole brain could be examined; in 6 cases only a specimen obtained at operation had been examined. The history of these 8 cases ranged from 3 months to 19 years; all patients except one showed clinical signs of hypopituitarism. Radiologically, in 4 cases there was enlargement of the sella and in 4 cases there was a normal or nearly normal sella. All patients of this series showed a suprasellar extension of the tumour.

The author considers that the majority of suprasellar tumours, hitherto regarded as chromophobe adenomata, are gliomata of the neural part of the hypophysis or of the pituitary stalk; he is, of course, fully aware that his own observations are not yet sufficient to draw final conclusions, but believes that the whole problem of pituitary lesions should be re-examined. *F. K. Kessel*

2513. **Bilateral Extensive Focal Ischemic Atrophy of the Kidneys**

H. R. CHRISTOFERSEN and E. F. HIRSCH. *Archives of Pathology* [*Arch. Path.*] **48**, 548–556, Dec. 1949. 4 figs., 29 refs.

A white woman of 35 had migratory polyarthritis in the fifth month of her second pregnancy. After delivery of a full-term child her blood pressure was 162/110 mm. Hg and there was slight albuminuria. Three days later the urine contained albumin, many granular casts, and a few erythrocytes. The blood pressure rose to 184/120 mm. Hg. Thirty-three days after delivery she returned to hospital with signs of cardiac decompensation. Two days later there developed evidence of femoral arterial occlusion and the urine contained much albumin and granular, waxy, and cellular casts. The non-protein nitrogen content of the blood on the following day was 91 mg. per 100 ml. Embolectomy of the right femoral artery was performed and spinal analgesia was continued after operation. Forty days post partum the patient died following cardiac and progressive renal failure.

The necropsy findings included: subacute puerperal uterine endometritis; thrombosis of the veins of the broad ligament; mural thrombi of the heart chambers and "bilateral extensive focal atrophy of the cortex of the kidneys; obturator thrombi of the left renal vein and of one of the two right renal arteries." The kidneys weighed 155 and 165 g. respectively. The surfaces were finely granular, red-brown, with "scattered plateaus of a grey-yellow tissue, elevated 2 to 3 mm. above the red-brown portions". The grey-yellow areas varied from 1 mm. to 2 cm. in diameter and were roughly wedge-shaped, extending through the cortex, but not into the medulla. In these areas the glomeruli were prominent; the afferent arterioles were not thickened, and the vessels were patent; the efferent vessels were dilated with blood cells. Occasional intralobular arteries were slightly cuffed with lymphocytes, plasma cells, and polymorphonuclear leucocytes. Some interlobular arteries showed fibrous thickening of the intima, with intact internal elastic membranes. A few of the convoluted tubules had flattened lining cells, and granular precipitates within their lumina. The collecting tubules had "the usual low columnar lining" and contained amorphous precipitates. In the depressed cortical areas the glomeruli were shrunken, with small capillaries and cellular and contracted tufts; a few were hyalinized. At all levels the tubules were atrophic. Interstitial tissue was not increased. The afferent arterioles were thin-walled, and around the patent intralobular arteries there were perivascular collections of inflammatory cells. There was fibrous thickening of the intima of many of the arcuate and interlobar arteries, some being completely occluded. The lumina of some larger branches of the renal vein were occluded by organized thrombi.

The literature is reviewed. Bilateral focal ischaemic atrophy of the renal cortex associated with thrombotic or fibrous occlusion of intrinsic branches of the renal arteries has been reported in lupus erythematosus disseminatus, scleroderma, rheumatic fever, periarteritis nodosa, and "possibly syphilitic endarteritis". The renal lesions consist essentially of depressed areas of severely ischaemic cortical tissue contrasting with plateau-like regions of nephrotic tissue. The authors consider that the occlusion of the vessels is due to injury the nature of which is unknown. Renal function is reduced progressively as a result of the vascular lesions, and death in uraemia follows. *B. G. Maegraith*

2514. **The Morphology and Pathology of the Ligamentum Flavum.** (Zur Morphologie und Pathologie des Ligamentum flavum)

W. HERZOG. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **61**, 250–267, 1949. 10 figs., 28 refs.

The ligaments of the spine, especially the ligamenta flava, of 68 cases at necropsy were examined in order to discover whether, and in what degree, pathological changes in them may be responsible for sciatica-like symptoms. The elastic fibres of the ligamenta flava show degenerative changes (hyalinization, fatty degeneration) so frequently that these are apparently normal changes caused by age. The thickness of the ligamenta flava varies greatly in individual cases, up to 9 mm.; the author is therefore very sceptical of the view that an increase in thickness causes sciatic pain. In 5 cases in which herniation of the nucleus pulposus was present there were no clinical symptoms during the patient's lifetime. In one case, a metastasis of a lymphosarcoma was found. *O. Neubauer*

2515. **A Study of the Germinal Epithelium in Male Paraplegics**

G. N. STEMMERMANN, L. WEISS, O. AUERBACH, and M. FRIEDMAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 24–34, Jan., 1950. 6 refs.

In routine necropsies on 4 patients dying after a long period of paraplegia the authors found severe testicular tubular atrophy with maturation arrest in 2, and a less severe degree of atrophy in a third. They then carried out surgical testicular biopsy on 16 paraplegic volunteers between the ages of 23 and 36. Biopsy specimens were taken under thiopentone anaesthesia (14 cases) or local procaine analgesia (2 cases). The specimens were 3 to 5 mm. in diameter: one-half of each was fixed in Zenker–acetic or Bouin's fixative, embedded in paraffin, and the sections stained with haemalum and eosin, the other half being fixed in Baker's calcium–cadmium–formol fixative and frozen sections stained with Sudan black B. Microscopically, 10 out of the 16 specimens showed severe maturation arrest. The tubules in these cases contained Sertoli cells with or without spermatogonia and spermatocytes, but no significant number of spermatids or spermatozoa. Fibrosis of the basement membrane or the interstitial tissue was not seen and there was no significant alteration in the distribution or quantity of stainable fat.

The authors discuss the relation of the testicular changes to local disease (epididymitis or urinary infection), to systemic disease (general infections and nutritional disturbances) and to the paraplegia. They

conclude that since both local and general disease could be excluded as significant causes in this series, deprivation of nerve supply is the probable cause of atrophy of the testis in paraplegia, though the mechanism by which it acts is not clear. *C. V. Harrison*

2516. **The Histology of the Lesions Caused by the Sting of the Hive-Bee (*Apis mellifica*)**
W. CREWE and R. M. GORDON. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **43**, 341–344, Dec., 1949. 4 figs., 24 refs.

2517. **The Liver in Infectious Mononucleosis: Histological Study by Means of Needle Biopsy.**
L. BERTRAND. *Presse Médicale* [*Pr. méd.*] **57**, 1218–1220, Dec. 25, 1949. 14 figs., 17 refs.

CLINICAL PATHOLOGY

2518. **Bronchial Carcinoma. A Practical Method of Early Diagnosis**
K. R. CROSS, T. E. CORCORAN, T. J. COOPER, and S. N. LANDIS. *Archives of Pathology* [*Arch. Path.*] **48**, 491–502, Dec., 1949. 4 figs., 34 refs.

After a brief survey of the literature concerning the diagnosis of bronchial carcinoma by the examination of sputum and bronchial washings, the authors describe the technique which they use at the U.S. Veterans Administration Hospital, Des Moines, Iowa. Material aspirated during bronchoscopy (undertaken primarily for biopsy purposes) is immediately put into formalin. In the laboratory it is then centrifuged at 1,000 to 2,000 revolutions per minute for 10 to 45 minutes and, after at least 4 hours' fixation, the deposit (wrapped in filter paper if necessary) processed by routine methods and embedded in paraffin. Sections are cut at four different levels and stained with haematoxylin and eosin. A total of 101 specimens were examined from 81 patients, 24 of whom were later proved to have bronchial carcinoma. Of the findings in these 24 cases on examination of the bronchial washings, those in 10 cases were definitely positive, in 3 strongly suggestive, and in 2 suggestive. Of the last 10 positive cases in this series 9 were diagnosed by means of this aspiration procedure.

Peter Harvey

2519. **Liver Biopsy as an Aid to the Diagnosis of the Cause of Enlargement of Hilar and Mediastinal Lymph Nodes.** (De leverbiopsie als hulpmiddel bij de diagnose van vergrote klieren in de longhilus en het mediastinum)
C. VAN BEEK and A. J. C. HAEX. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 3465–3469, Oct. 8, 1949.

Biopsy of the liver was performed as a diagnostic procedure in 47 patients with enlarged hilar lymph nodes of uncertain aetiology (Boeck's sarcoid, tuberculosis). In 30 of these, tubercle-like structures were found in the biopsy material. The principal clinical features and the case histories of these 30 patients are summarized in a table. Von Pirquet's reaction was positive in 17 and the Mantoux test in 8 cases, the spleen was palpable in 15 cases, and the liver considered to be enlarged in 6. Peripheral lymph-node enlargement was noted in 9 patients. The temperature was normal in 10 patients, slightly raised in 15, and markedly raised in 5. In over 100 control cases (patients without any signs of tuberculosis or Boeck's sarcoid), tubercle-like structures were never seen on liver biopsy. In one patient with enlarged hilar nodes, thought to be of a tuberculous nature, liver biopsy was negative; later on the patient proved to be suffering from Hodgkin's disease. The authors particularly stress the point that in liver biopsies it is quite impossible to distinguish between the histological appearances of tuberculosis and those of Boeck's sarcoid unless the former show the characteristic central necrosis.

E. Kits van Waveren (*Excerpta Medica*)

2520. **The Laboratory Diagnosis of Lymphogranuloma Venereum**
S. P. BEDSON, C. F. BARWELL, E. J. KING, and L. W. J. BISHOP. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 241–249, Nov., 1949. 14 refs.

Lymphogranuloma venereum is diagnosed by the finding of the specific virus, but, as this is a time-consuming procedure, the authors have re-investigated the value of the Frei test and the complement-fixation reaction.

The antigen for the complement-fixation test was prepared from yolk-sac cultures, and was subjected to steaming, which destroyed the heat-labile antigenic components. With such an antigen a positive complement-fixation test at 1 in 32 was obtained in 87·5% of 32 cases in which a " confident " clinical diagnosis had been made, in 22·6% of 31 cases in which the diagnosis was " possible ", and in 1·5% of cases in which the clinical diagnosis was " doubtful ". Thus the serological findings showed quite a close correlation with the clinical diagnosis.

The effective antigen in this complement-fixation test is the heat-stable one also found in psittacosis, so that the test is positive also in cases of the latter disease.

Psittacosis virus contains a heat-labile antigen in addition to the stable group-specific component, and there is evidence that the viruses of psittacosis and lymphogranuloma venereum each possess a specific antigen detectable by neutralization tests made with antisera produced in the domestic fowl. Neutralization tests made with human and mammalian sera give no such clear-cut specificity, however. But there is some evidence that mammalian anti-psittacosis sera do contain antibody to the labile antigen, so an attempt was made, on analogy, to demonstrate complement fixation with fresh, unheated lymphogranuloma venereum virus. No success was obtained.

It has been shown that if a psittacosis antiserum made in the guinea-pig be absorbed with steamed psittacosis antigen, the corresponding antibody is removed, leaving only the antibody to the heat-labile antigen, whereas absorption with the unheated virus removes both. Thus in the same way treatment of serum from a patient with lymphogranuloma venereum with steamed virus

should remove its ability to react not only with the steamed homologous virus, but also with both forms of heterologous virus. This the authors found to be the case.

The Frei test was also carried out in the great majority of the cases examined serologically, the effective antigen again being a heat-stable one. There was a close parallelism between the Frei reaction and the complement-fixation reaction in the clinically positive group; in a considerable number of doubtful cases of lymphogranuloma venereum there was a strongly positive Frei reaction but there was little or no antibody in the serum. These were thought to be old cases in which the disease was now quiescent.

As was anticipated, intracutaneous tests made with steamed psittacosis virus on 39 patients gave similar results to that of the Frei test. An attempt was made to elaborate a specific skin reaction by treating suspensions of psittacosis virus and lymphogranuloma venereum virus with acid, in order to inactivate the heat-stable components. Parallel tests were then carried out in a small number of cases. While the acid-soluble antigen of psittacosis virus failed to produce a reaction in these cases of lymphogranuloma venereum, the homologous extract elicited a definite response. In one case of psittacosis the results of using these preparations were equally specific. *R. B. Lucas*

2521. **Plasma Prothrombin Times in Normal Human Subjects. The Effect of Certain Factors on the Prothrombin Time**
R. S. OVERMAN, A. A. NEWMAN, and I. S. WRIGHT. *American Heart Journal* [*Amer. Heart J.*] **39**, 56–64, Jan., 1950. 14 refs.

The authors describe in detail the Link–Shapiro modification of Quick's one-stage test for determining plasma prothrombin times. More than 800 determinations have been made by this method and the influence of various factors on the prothrombin time has been studied. They conclude that it is probably not necessary that blood for prothrombin tests be taken with the patient fasting and at rest. *R. T. Grant*

2522. **The Prothrombin Consumption Test. Its Clinical and Theoretic Implications**
A. J. QUICK and J. E. FAVRE-GILLY. *Blood* [*Blood*] **4**, 1281–1289, Dec., 1949. 17 refs.

The authors believe that the auto-catalytic nature of blood coagulation depends upon the fact that a constant supply of thrombin is necessary for the disintegration of platelets. In the present paper they show that only a minute amount of prothrombin is converted to thrombin in the coagulation of all the fibrinogen of the blood. The prothrombin level then remains constant until the serum is separated from the clot mechanically or by retraction; thereafter the prothrombin content decreases rapidly. The authors believe that all free thrombin is adsorbed on to the large fibrin surface of the intact clot; thus platelets, without thrombin, cannot disintegrate to activate more thromboplastin. " Obviously fibrin, itself, is the most important physiological antithrombin."

The authors investigated this phenomenon by centrifuging blood at varying intervals after clotting and estimating the prothrombin time of the serum by Quick's method. Prothrombin consumption during centrifugalization was prevented by adding sodium citrate. They thus measured the conversion of prothrombin both in clotted blood and in clot-free serum, and concluded that: " The prothrombin consumption shows considerable variations in normal individuals. In haemophilia and in thrombocytopenia it is very incomplete. In hypoprothrombinaemia the prothrombin [consumption] may be very complete as in congenital hypoprothrombinaemia of the component A deficiency type, or surprisingly incomplete as in dicoumarol hypoprothrombinaemia."
Martin Hynes

2523. **An Improved Method of Counting Blood Platelets and its Evaluation in Blood of Rabbits**
G. J. SCHEFF and P. H. RALPH. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 1113–1121, Dec., 1949. 1 fig., 7 refs.

2524. **Urea Clearance Tests**
H. F. SMITH. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 266–272, Nov., 1949. 1 fig., 20 refs.

These investigations were carried out on 65 men in a prisoner-of-war hospital in Siam.

In each case observations were made of the amount and concentration of urea nitrogen in the urine excreted during each of 2 successive hours after a breakfast of rice and weak tea. One sample of blood was taken about the middle of the 2-hour period. The precise amount of protein in the diet was unknown, but was very low—in the region of 25 to 86 g. per day.

Despite difficult laboratory conditions the observations were of the same degree of accuracy as those in previously published work. The variance of log U from its regression on V and B was, for the normal group of 15 cases, 0·00263, compared with a corresponding figure for the data of McIntosh *et al.* (*J. clin. Invest.*, 1928, **6**, 467) of 0·00243.

Comparison of the results with previously published figures for a group of residents in the U.S.A., who had, presumably, fairly high protein diets, and for a group of Indians on a moderate to low protein diet, showed certain notable features. Thus when the diet is altered but the body is given time to readjust its balance to the new conditions, as in the prisoners of war, the blood urea concentration is maintained at the same level as usual, in Europeans about 15 to 16 mg. per 100 ml. Thus the blood urea concentration does not respond to a permanent alteration in protein intake in the same way as it does temporarily to a dose of urea, and so in individuals on permanently different diets the blood urea levels tend to be approximately constant, while the urea concentration in the urine varies to allow for the differences in amount of urea excreted. This being so, it can be seen that the statement " renal efficiency is low " really means " the ratio of urine urea to blood urea concentration is low compared with the ratio observed in a small group of Americans " (Van Slyke's original patients). Thus the author claims that an extremely

low clearance (C_s=10, or 18%) may have nothing to do with renal efficiency, being the result of a low-protein diet.

The author discusses the statistical basis of the Van Slyke clearance test, for details of which the original paper should be consulted. *R. B. Lucas*

2525. **The Significance of the Urea Clearance**
D. D. VAN SLYKE and V. P. DOLE. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 273–274, Nov., 1949. 18 refs.

This paper is a reply to criticisms of the urea clearance test which were made by Smith (see Abstract 2524) on the basis of results obtained in a Far East prisoner-of-war camp, where very low clearance values were obtained in persons with normal kidneys, the cause being the low amount of protein in the diet.

The authors point out that by the urea clearance test the efficiency with which the kidneys remove urea from the blood stream is measured, and that studies in man and animals have shown that the urea clearance indicates the rate of filtration of urea in the glomeruli minus the rate of urea reabsorption by the tubules. Smith had held that the statement " renal efficiency is low " really meant nothing more than " the ratio of urine urea to blood urea concentration is low compared with the ratio observed in a small group of Americans ".

Furthermore, there is the question of variation in normal persons, since the urea clearance behaves like all physiological functions in this respect. Neither the urea clearance, nor any other physiological function, the authors state, should serve as the sole criterion in discriminating between health and disease. The results must be evaluated in terms of all known causes of variation, physiological and pathological. As the increase in metabolic rate with activity or excitement does not invalidate use of its measurement in the thyroid clinic, so the decrease in urea clearance with protein starvation or shock does not render its employment invalid in following the course of renal damage or disease, when due allowance is made for the effect of extrarenal influences. *R. B. Lucas*

2526. **Some Investigations with the " Glass Tube Method " of Urine Analysis.** (Nogle undersøgelser med " glasrørsmetode " ved urinanalyser)
P. E. OSWALD and G. SEIDELIN. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **112**, 108–111, Jan. 26, 1950. 3 figs., 5 refs.

The senior author has described (*Ugeskr. Læg.*, 1949, **111**, 188) a simplified method of testing for urinary protein. A fine glass tube of 3 to 4 mm. diameter is dipped into the sample, the upper end is closed with the finger, and the tube is withdrawn and dipped into 25% nitric acid. A white precipitate appears at the junction of the two fluids if protein is present. He has now developed the method for laboratory and private use by designing a " perspex " battery holding 10 (or 18) fine test-tubes which are filled up to the mark with nitric acid. With this battery large numbers of tests can be performed very rapidly, and if the correct technique is used the nitric acid remains uncontaminated and can be used indefinitely. The same principle can be applied to other protein tests, to the benzidine test, to the Griess test, to the ferric chloride test, and to the silver nitrate test for chloride (but in this last case the method is almost too sensitive). The method is not suitable for iodine reactions with bile pigments. *B. Nordin*

2527. **Clinical Evaluation of Various Tests for Occult Blood in the Feces**
S. O. HOERR, W. R. BLISS, and J. KAUFFMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 1213–1217, Dec. 24, 1949. 3 figs.

In this study three tests for occult blood in the faeces were used, the benzidine, *ortho*toluidine, and guaiac tests, the purpose being to determine the value of such investigations in the diagnosis of malignant lesions in the gastro-intestinal tract. None of the patients was subjected to any dietary restrictions not imposed by the nature of the illness, and " stools were taken as they came ".

The three reagents were tested *in vitro* for sensitivity to blood. At 60 seconds benzidine gave a positive reaction with blood in 1 in 100,000 dilution, *ortho*toluidine with a 1 in 20,000 dilution, and guaiac with dilutions from 1 in 1,000 to 1 in 5,000.

Equal quantities of blood were mixed with samples of human gastric juice and with isotonic sodium chloride solution. The mixtures were incubated at body temperature for an hour and were then tested quantitatively for occult blood. Proportionately larger amounts of the gastric juice mixture were required to produce a positive result than of the saline controls, showing that *in vitro* there is a partial inactivation of the blood by the action of gastric juice. It was also verified that ferrous sulphate taken orally in sufficient amount to produce a black stool will cause a weakly positive guaiac test.

The material for the investigation consisted of 264 stools from 140 unselected hospital patients. In the first instance, stools from 92 patients were tested, when it was found that 95% of the specimens were positive by the benzidine test, 87% by the *ortho*toluidine test, and 22% by the guaiac test. It was therefore concluded that the benzidine and *ortho*toluidine tests were much too sensitive for routine use in a screening test on patients who had not been given a special diet, since only a small proportion of these 92 patients later proved to have any organic gastro-intestinal disease.

Attention was now focused on the guaiac test. There were 39 positive results in tests from 140 patients, 5 of whom were later found to have an ulcerative malignant gastro-intestinal lesion, and 26 of whom had other good clinical cause for a positive result. In 8 cases no reason for the positive reaction was found. Among the 101 patients with negative reactions 3 had an ulcerative malignant gastro-intestinal lesion.

The authors conclude that a positive guaiac reaction denotes organic bleeding in a high proportion of cases, but that a negative reaction does not rule out organic disease of the gastro-intestinal tract, including malignant growth. They also describe a simplified, but reliable, modification of the test, suitable for use in the surgery.
R. B. Lucas

Microbiology

2528. **An Electron Microscope Study of Nerves Infected with Human Poliomyelitis Virus**
E. DE ROBERTIS and F. O. SCHMITT. *Journal of Experimental Medicine* [*J. exp. Med.*] **90**, 283–289, Oct. 1, 1949. 9 figs., 14 refs.

2529. **An Electron Microscope Analysis of Nerves Infected with the B Virus**
E. DE ROBERTIS. *Journal of Experimental Medicine* [*J. exp. Med.*] **90**, 291–295, Oct. 1, 1949. 9 figs., 10 refs.

2530. **Resistance to the Lymphogranuloma Venereum Virus in the Mouse caused by *Encephalitozoon cuniculi*.** (Résistance au virus de la lymphogranulomatose vénérienne engendrée chez la souris par *Encephalitozoon cuniculi*)
P. LEPINE and V. SAUTTER. *Annales de L'Institut Pasteur* [*Ann. Inst. Pasteur*] **77**, 770–772, Dec., 1949. 3 refs.

Mice with cysts due to *Encephalitozoon cuniculi* in the central nervous system failed to develop the lesions of lymphogranuloma venereum when its virus was injected intracerebrally. Mice uninfected with *E. cuniculi* developed extensive lesions with two strains of lymphogranuloma venereum virus. *G. M. Findlay*

2531. **The Apparent Inactivation of Vaccinia Virus by Heat-treated Penicillin *in vitro* and *in vivo*.** (Kann das Vaccine-virus durch gekochtes Penicillin *in vitro* und *in vivo* inaktiviert werden?)
B. FUST and P. GRÜNIG. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **130**, 269–274, 1949. 4 refs.

The authors, working at the Swiss Serum and Vaccine Institute, Berne, have studied the effect *in vivo* and *in vitro* of heated penicillin on the activity of vaccinia virus in rabbits. Penicillin preparations, diluted to contain 10,000 units per ml., were heated at 100° C. for various periods of time, cooled, mixed with serial dilutions of virus, and applied to the epilated skin of rabbits. Heated penicillin reduced the infectivity of the virus at least 100-fold, but unheated penicillin was without effect. Crystalline penicillin G and one commercial preparation developed maximum inhibitory activity after heating for 15 minutes; another commercial preparation required heating for 2 hours. The effect *in vivo* was examined by inoculating 0·2 ml. (2,000 units) of heated penicillin intradermally, dilute virus then being applied with scarification immediately over the inoculation site. The number of pustules developing was reduced to approximately one-third of that found in control animals. When rabbits were given daily intravenous injections of heated penicillin (total 400,000 units) for 7 days after the application of virus to the skin the onset of infection was retarded as long as administration continued. On withdrawal of penicillin, however, typical pustules developed. Apart from a slight reduction in fever no similar effect was observed when this experiment was repeated with crystalline penicillin G.

[It is evident that the inactivation of virus *in vitro* is due to an impurity in commercial penicillin, as was noted for canary-pox by Groupe and Rake (*J. Immunol.* 1947, **57**, 17). The significance of the experiments *in vivo* is questionable.] *J. F. McCrea*

2532. **A Comparison of the Bacterial Flora of the Pharynx and Nasopharynx**
J. H. DINGLE, T. J. ABERNETHY, G. F. BADGER, J. W. BEARD, N. L. CRESSY, A. E. FELLER, I. GORDON, A. D. LANGMUIR, C. H. RAMMELKAMP, E. STRAUSS, H. TATLOCK, and N. PLUMMER. *American Journal of Hygiene* [*Amer. J. Hyg.*] **50**, 331–336, Nov., 1949. 3 refs.

The initial purpose of this work was to decide whether nasopharyngeal or pharyngeal (pharynx and tonsillar area) swabs gave the most suitable sample of the flora of the upper respiratory tract. Nasopharyngeal swabs revealed the presence of *Staphylococcus aureus* and *Haemophilus influenzae* more frequently than did pharyngeal swabs, but *Streptococcus pyogenes* was found with the same frequency in both. Of greater importance was the finding that a duplicate swab adds greatly to the value of either method. One swab may give a misleading indication of the flora and many carriers of *Strep. pyogenes*, for example, would be missed unless a second were taken. *Scott Thomson*

2533. **Isolation of Salmonellae from Dogs, Cats, and Pigeons**
J. C. CRUICKSHANK and H. W. SMITH. *British Medical Journal* [*Brit. med. J.*] **2**, 1254–1258, Dec. 3, 1949. 38 refs.

Faeces from 500 dogs, 500 cats, and 133 pigeons in London were examined for the presence of salmonellae. The organisms were isolated from 5 (1%) of the dogs (*Salmonella newport*, 2; *Salm. typhimurium*, 2; unidentified, 1); from 7 (1·4%) of the cats (*Salm. typhimurium*, 3; *Salm. anatum*, 2; *Salm. montevideo*, 1; *Salm. paratyphi B*, 1); and from 3 (2·25%) of the pigeons (*Salm. typhimurium*, 3). A discussion follows, on the significance of the presence in domestic animals of salmonellae of types responsible for disease in man.
Joyce Wright

2534. **The Action of Streptomycin. I. The Nature of the Reaction Inhibited**
E. L. OGINSKY, P. H. SMITH, and W. W. UMBREIT. *Journal of Bacteriology* [*J. Bact.*] **58**, 747–759, Dec., 1949. 7 figs., 18 refs.

These experiments were carried out on resting-cell suspensions of the "Gratia" strain of *Bacterium coli* to test the hypothesis that the terminal respiration

process in *Bact. coli* involves a pyruvate–oxalacetate condensation and that streptomycin exerts its effect in relation to this. Oxalacetate was prepared from sodium diethyloxalacetate and recrystallized from acetone–benzene mixtures. Keto-acids were determined by the method of Friedmann and Haugen (*J. biol. Chem.*, 1943, **147**, 415). All respiration studies were made at 37° C. in 0·003 M phosphate buffer at *p*H 7. The organisms were grown in 1 litre Erlenmeyer flasks containing 800 ml. of medium consisting of 1% each of " difco " tryptone and yeast extract and 0·5% K_2HPO_4 in distilled water. After 16 to 18 hours' incubation at 37° C. the cultures were centrifuged and the cells, after washing, suspended in distilled water to give 0·5 mg. bacterial nitrogen per ml. Grown under these conditions the resting-cell suspensions oxidize added pyruvate, apparently to acetate, and fresh suspensions (less than 2 or 3 days old) possess an active oxalacetate decarboxylase which rapidly converts added oxalacetate to pyruvate. Study of the oxidation of oxalacetate and pyruvate with and without 20 μg. streptomycin per ml. showed that added oxalacetate is initially oxidized at a slower rate than pyruvate; without streptomycin the rate then gradually increases; with streptomycin it remains constant. Since oxalacetate cannot be oxidized as such, it was thought that either it was first decarboxylated and the resulting pyruvate oxidized or it condensed with pyruvate to enter a " citric acid cycle ". The increasing rate of oxidation, therefore, could be due to the occurrence of the oxalacetate–pyruvate condensation reaction and it would then be likely that streptomycin inhibited this.

In older cell suspensions, oxalacetate is not rapidly converted into pyruvate. In oxidation studies of such suspensions, it was found that pyruvate is oxidized normally, but oxalacetate only very slowly. When a mixture of oxalacetate and pyruvate was added, the oxygen uptake was considerably greater than with either alone (suggesting the condensation reaction), and this increase was inhibited by streptomycin. In these experiments there was, however, a lag period; the pyruvate was not, therefore, oxidized as rapidly in the presence of oxalacetate as when added alone. Keto-acid analyses showed that pyruvate, whether added alone or with oxalacetate, disappears rapidly during this lag period. When both are added, for every mole of pyruvate lost a mole of oxalacetate disappears, with hardly measurable oxygen uptake. This disappearance of keto-acids was not influenced by streptomycin. Theoretical considerations led to the conclusion that oxalacetate in the presence of pyruvate can act as a hydrogen acceptor leading to the formation of malate and fumarate, and that thus the addition of malate or fumarate to cell suspensions would yield similar results without a lag period. This was confirmed experimentally.

It was further shown that in the presence of streptomycin oxygen uptake was sufficient only for oxidation to acetate, whereas without streptomycin oxidation proceeded much further. This could be due to the prevention of the oxalacetate–pyruvate condensation by streptomycin or interference by the antibiotic with the metabolism of " active acetate ". Further experiments, though not absolutely conclusive, favoured the former view.

In other experiments it was found that about 30 minutes' contact between the cells and streptomycin was necessary before streptomycin was fully effective. This time period was thought to be necessary to permit diffusion of streptomycin into the cell. After 30 minutes' exposure the reaction was not reversible.

The inhibition of this reaction was regarded as specific, as antibacterial derivatives of streptomycin had a similar action whereas derivatives without antibacterial effects did not inhibit the reaction. *Mary Barber*

2535. **The Action of Streptomycin. II. The Metabolic Properties of Resistant and Dependent Strains**
P. H. Smith, E. L. Oginsky, and W. W. Umbreit. *Journal of Bacteriology* [*J. Bact.*] **58**, 761–767, Dec., 1949. 2 figs., 7 refs.

This paper is concerned with the metabolic reactions of strains of *Bacterium coli* resistant to or dependent on streptomycin. The strains came from two streptomycin-sensitive parent cultures, " Murray " and " Gratia ". The resistant variants were inhibited only by 35,000 μg. per ml. (Murray) and 20,000 μg. per ml. (Gratia). The lowest concentration of streptomycin permitting growth of the dependent variants in a synthetic medium (containing glucose, ammonium sulphate, K_2HPO_4, and inorganic salts) was slightly over 10 μg. per ml. The methods used were those of the previous paper (Abstract 2534).

The sensitive parent strains benefited by the presence of air during growth, were able rapidly to oxidize the intermediates of the citric-acid cycle, and possessed an enzyme causing the oxalacetate–pyruvate condensation. The resistant variants did not have these properties. In the first experiment, growth was studied after 48 hours at 37° C. in a yeast-extract–tryptone medium with increasing quantities of glucose under two conditions; first in flasks well filled with medium in which the incubation of air was limited, and secondly in cultures shaken to give vigorous aeration. The sensitive strains showed a 10-fold increase in growth when aerated; the resistant cultures responded little or not at all to aeration.

In the second experiment the ability of the strains to oxidize the components of the citric-acid cycle was studied. The degree of oxidation of all the substrates tested was considerably less in the case of the resistant variants than it was with the sensitive strains.

Oxidation of pyruvate, oxalacetate, and mixtures of the two by the sensitive cultures proceeded in a manner similar to that previously described. With the resistant variants, however, oxalacetate and pyruvate were oxidized no faster than oxalacetate alone, and therefore the oxalacetate–pyruvate condensation was apparently absent.

Similar experiments with the dependent strains showed less difference between them and the sensitive cultures. Thus both sensitive and dependent organisms responded to aeration by increase in growth, and some of the dependent variants oxidized the intermediates of the citric-acid cycle. The dependent strains, however, did not possess the oxalacetate–pyruvate reaction. Oxalacetate

was oxidized much more quickly by the dependent than by the sensitive cells. This is explained on the hypothesis that with the dependent cells the oxalacetate is decarboxylated to pyruvate and the latter oxidized to acetate without a condensation occurring between them.

The authors thus suggest that the resistant and dependent variants they have studied are resistant to streptomycin because the oxalacetate–pyruvate condensation reaction has been eliminated, thus " by-passing " the site of inhibition of the antibiotic. So far further experiments to establish this hypothesis have proved unsuccessful. *Mary Barber*

2536. **Classification of the Streptococci of Subacute Bacterial Endocarditis**
J. S. PORTERFIELD. *Journal of General Microbiology* [*J. gen. Microbiol.*] **4**, 92–101, Jan., 1950. 24 refs.

2537. **Investigation of Fungi in Hanging Drop Cultures. Preliminary Report**
A. A. ZIMERINOV and S. M. RAFALOVICH. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **61**, 94–104, Jan., 1950. 9 figs.

2538. **Chemical and Immunological Properties of Diphtheria Toxoid Purified by Ammonium Sulfate Fractionation**
L. LEVINE, L. WYMAN, and G. EDSALL. *Journal of Immunology* [*J. Immunol.*] **63**, 219–232, Nov., 1949. 3 figs., 19 refs.

The increasing incidence of diphtheria in adults, noticeable in many countries at the present time, has focused attention on adult immunization. Rather severe reactions to the usual agents are not uncommon in adults, due to increased sensitivity either to the diphtheria-toxoid protein or to other proteins present in culture filtrates. For this reason the manufacture of purified toxoid preparations is of some importance. The authors of this paper have endeavoured to work out a relatively simple method for the purification of a relatively pure diphtheria toxoid derived from cultures grown on the semi-synthetic medium of Mueller. Further purification is carried out by a simple three-step precipitation and fractionation of the proteins of the crude toxoid with ammonium sulphate at room temperature and at a *p*H of 6·5, the total protein content of the crude toxoid being 0·4 to 0·5 g. per litre. The resulting concentrated antigen is then made isotonic and diluted with an equal volume of saline solution for storage. It is further diluted for clinical use with a sterile, $\frac{1}{15}$-molar, phosphate solution made isotonic by addition of 0·4% NaCl. Purity is assessed by assaying the Lf units per mg. of protein nitrogen and comparing this value with the value for pure toxoid (approximately 2,170 Lf per mg. N). On this basis, the purity achieved in the various batches of toxoid varies between 51 and 93%, and preparations with a toxoid content of more than 2,000 Lf per mg. N are obtained.

When doses of crude and purified toxoid of equal Lf value were injected into guinea-pigs, the purified toxoid gave better protection against subsequent injection of 10 MLD of diphtheria toxin. It was further shown that the purified toxoid had a shorter flocculation time than the crude toxoid. This is probably due to the fact that non-flocculating proteins, eliminated in the purifying process, have an inhibiting effect on flocculation *in vitro*. Evidence is produced for a linear relationship between flocculation time and titre at the toxoid–antitoxin equivalence point.

It is stated in an addendum that the purified toxoid (2 batches) has been used to immunize 1,172 [? adult] persons. The incidence and severity of side reactions did not differ significantly from those observed after injection of toxoid prepared by methanol precipitation, and the serum antitoxin level in a small number of subjects bled after 3 to 4 weeks was at least as high as in individuals immunized with other preparations.

K. S. Zinnemann

2539. **Specific Serological Reactions Which Follow Naturally Acquired Mumps**
A. L. FLORMAN and J. H. KUTCH. *Journal of Immunology* [*J. Immunol.*] **63**, 281–289, Nov., 1949. 2 figs., 14 refs.

For demonstration of the presence of mumps virus in the serum, four methods are available: (1) a complement-fixation reaction with the mumps virus, grown in the chick embryo, as antigen; (2) a complement-fixation reaction with a soluble antigen from infected allantoic membranes; (3) the agglutination-inhibition test, in which agglutination of human or fowl erythrocytes by a laboratory strain of mumps virus is inhibited by the patient's serum; and (4) agglutination by convalescent serum of human erythrocytes previously treated with a laboratory strain of mumps virus. All these tests were carried out on sera collected on at least two occasions from 8 patients with naturally acquired mumps in an attempt to determine at what stage of the infection antibodies may first be detected and which of the tests is the most reliable. Investigations were started on the 2nd or 3rd day of disease and were continued up to the 14th day. In one case, however, in which antibodies appeared only during the 2nd week, the period of investigation was extended until the 24th day.

Marked individual variations were noted. In 6 of the 8 patients one of the 2 complement-fixation tests was the first to give a positive result, while in the other 2 patients the agglutination-inhibition test was the first, complement-fixing antibodies appearing rather late in the course of the infection. After 2 weeks the serum of all 8 patients gave a positive reaction in 2 or more of the tests. The titres of the antibodies and their time of appearance seemed to be unrelated to the severity of illness. The tests may be of value in patients suspected of mumps without any of the classical symptoms being present.

[For details of technique the original paper should be consulted.] *K. S. Zinnemann*

2540. **Typhoid Fever Prophylaxis by Active Immunization**
H. C. BATSON. *Public Health Reports. Washington* [*Publ. Hlth Rep., Wash.*] Suppl. 212, 1–34, Aug., 1949. Bibliography.

Paediatrics

2541. **Hyaluronidase in Administration of Fluids**
A. A. JAWORSKI and J. E. FARLEY. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 59–64, Jan., 1950. 9 refs.

Exhaustive investigations were carried out on 10 healthy children before, during, and after the daily subcutaneous administration of 25 (4 cases) or 250 (6 cases) viscosity units of hyaluronidase for 7 days. No changes were observed in the blood picture, blood chemistry, urine, results of liver function tests, electrocardiogram, or blood heparinoid activity. No local reactions occurred in this group, and the results of intradermal tests for sensitivity on a total of 150 patients were all negative. In 100 children the addition of 25 units of hyaluronidase to the fluid used for hypodermoclysis decreased to less than one-third the time taken for absorption of the same volume of fluid, and the injections were painless and the sites less swollen. There was no increase in the rate of absorption of the fluid with a tenfold increase in the dosage of hyaluronidase, nor was there any evidence of spread of infection locally or elsewhere by the hyaluronidase. This paper confirms previous reports of the absence of toxicity and the efficacy of hyaluronidase in facilitating the administration of fluids. *W. L. M. Turner*

2542. **Protein Requirements of Infants. 2. Marasmus**
W. F. YOUNG, E. A. BISHOP, E. M. HICKMAN, and Y. J. WILLIAMS. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **24**, 250–263, Dec., 1949. 8 figs., 26 refs.

The authors investigated 79 infants suffering from conditions leading to a fall in weight to 80% or less of that expected. The aim of treatment was to overcome protein depletion as soon as possible, and thus to lessen the danger of complications in the early stages of treatment. Cases investigated were divided into cases of complicated and uncomplicated pyloric stenosis and cases of marasmus due to other causes. The aim was to provide 120 Calories with 6 g. protein per kg. per day. The milk formula used as a basis for the early treatment was 12 oz. (336 ml.) lactic-acid milk (33% to 50%) in water, 6 drachms (21 ml.) " dextrimaltose ", and 9·6 g. casein hydrolysate, which gave a caloric value of 17 to 20 per oz. (28·4 ml.). The full strength of this mixture was given as soon as possible, continuing until the child was well on the way to recovery, when plain milk was substituted. Progress appeared to be made earlier than before and to be steadier.

Serum protein and haemoglobin levels were estimated weekly while the children were in hospital. Severe lowering of either level was rarely found. The serum protein level varied considerably from week to week and from case to case, but the general picture was similar to that previously found in animals recovering from malnutrition. Care must be taken to give the children an optimum diet until their weight is normal for their age group. This weight was estimated from work done on average weight-charting in Iowa by Jackson and Kelly. This return of weight to normal takes a long time and entails follow-up care after the infant has left the hospital.

[This article is meticulously prepared and fully documented. It is impossible to abstract with accuracy, and must be read in full. The cases of pyloric stenosis were all treated surgically and details of the dietary after-care are given.] *E. H. Johnson*

2543. **A Study of Ten Children After Treatment with Streptomycin for Tuberculous Meningitis**
J. LORBER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **24**, 289–293, Dec., 1949. 29 refs.

This article deals not with treatment, but with the follow-up study of the 10 successfully treated cases in a series of 27 cases of bacteriologically proved tuberculous meningitis. The shortest period of observation was 10 months from the onset of treatment with streptomycin, and all 10 children were physically well and had normal cerebrospinal fluid at the time of the report. Only one child was left with any physical defect, namely deafness, which is apparently complete except for appreciation of loud noises. Intelligence tests revealed a normal range of variation, and there was no evidence that the illness had resulted in any impairment of mental or emotional capacity. The author contrasts these findings with many previous and pessimistic reports of the sequelae encountered in patients surviving after tuberculous meningitis. *M. Baber*

2544. **Infectious Lymphocytosis. A Report of an Epidemic in Children**
B. K. LEMON and D. H. KAUMP. *Journal of Pediatrics* [*J. Pediat.*] **36**, 61–68, Jan., 1950. 18 refs.

Infectious lymphocytosis is a benign condition, characterized by marked leucocytosis and absolute lymphocytosis. It is infectious and contagious, with an incubation period of 12 to 21 days. Symptoms and signs may be minimal or may consist of vomiting, fever, morbilliform rash, abdominal pain, and occasionally nervous signs suggestive of poliomyelitis.

The authors describe an epidemic in a Detroit home for children aged 2 to 3 years. After the diagnosis of the disease in a child of 29 months, 49 out of a total of 106 children were investigated. In addition to a full history and clinical examination, erythrocyte sedimentation rate, liver function tests, Paul–Bunnell reaction, nose and throat cultures, and complete blood counts were studied. In cases with abnormal findings total and differential leucocyte counts were repeated at weekly intervals and chest radiographs were taken. Haematologically, the disease appears to fall into three phases;

(1) the acute phase, lasting for 2 to 3 weeks, in which the total leucocyte count was from 45,000 to 100,000 per c.mm. with 70 to 94% lymphocytes and a low eosinophil count; (2) the subsiding phase, lasting for 2 to 3 weeks, with a total leucocyte count of 18,000 to 60,000 per c.mm. and a lymphocyte count similar to that found in the acute phase, but with an eosinophilia of 5 to 20%; (3) the chronic phase, lasting for 7 to 12 weeks, in which the total leucocyte count is 8,000 to 16,000 per c.mm., with a high lymphocyte count falling to normal within 3 to 4 weeks and an eosinophil count gradually returning to normal. Bone-marrow studies carried out in 4 cases showed that the lymphocytes were small and mature and that numerically there was a rough correlation with the peripheral lymphocyte count. The differential diagnosis is from infectious mononucleosis and leukaemia. In the former disease there is lymph-node enlargement and a lower total leucocyte count with atypical lymphocytes and a positive Paul–Bunnell reaction. In leukaemia the lymph nodes are enlarged, bleeding occurs and is associated with thrombocytopenia, and immature lymphatic cells are found in the bone marrow.

R. M. Todd

2545. **Infant Salmonella Carriers**
I. M. MACKERRAS and V. M. PASK. *Lancet* [*Lancet*] **2**, 940–941, Nov. 19, 1949. 5 refs.

2546. **Duodenal Ulcers in Infants**
J. H. FISHER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 50–58, Jan., 1950. 5 figs., 10 refs.

The occurrence of peptic ulceration in childhood is well known, but rarely met with; 4 cases, all in males (aged 8 months, 6 weeks, 4 months, and 3½ months respectively), and all verified by necropsy are here described. The ulcers were multiple in 3 cases and showed the pathological features of a chronic penetrating peptic ulceration similar to that occurring in adults. The ulcers had perforated in 2 cases, giving rise to a localized peritonitis, and in one patient the ulcer was distal to the ampulla of Vater. The ulcer was acute in one child. The symptoms included anaemia, failure to thrive, melaena and frank blood in the stools, and diarrhoea and vomiting. No aetiological factors were discovered, but it is noted that all the infants were artificially fed.

W. M. L. Turner

2547. **Congenital Obstructions of the Alimentary Tract in Infants and Children: Errors of Rotation of the Midgut**
F. N. SILVERMAN and J. CAFFEY. *Radiology* [*Radiology*] **53**, 781–788, Dec., 1949. 4 figs., 8 refs.

During the fifth week of embryonic life the epithelial lining of the gut proliferates more rapidly than its surrounding walls. The lumen is occluded and replaced by a solid cord of cells. At the same time the elongation of the midgut is so marked that extrusion into the umbilical cord takes place. The causes of congenital alimentary-tract obstruction can thus be listed as follows: (1) Errors in recanalization lead to (*a*) transverse septa, plugs, and diaphragms; (*b*) longitudinal septal duplications; and (*c*) oesophageal atresia. (2) Errors in rotation as the gut is returned to the abdominal cavity may lead to (*a*) more or less severe volvulus; or (*b*) abnormal peritoneal bands. (3) Circular muscle hypertrophy. (4) Meconium ileus. (5) Intussusception.

Malposition or abnormal motility of the caecum on *x*-ray examination (preferably by barium enema) is regarded as evidence of malrotation, and the finding of abnormal peritoneal bands at operation confirms this. Many children with vague gastro-intestinal disturbances are thus thought to be victims of a congenital fault and to suffer from intermittent obstruction. Three case histories are given, one of which is typical and convincing. A boy aged 13 with a long history of attacks of pain and vomiting was found at operation to have the classical features of severe malrotation; division of peritoneal bands led to a cure and within 6 months he gained 45 lb. (20 kg.) and his entire personality changed.

[The diagnosis of intermittent obstruction is often obvious if straight radiographs are taken during an attack—a barium meal 24 hours later is generally useless. Cases of the type described are probably rare. When they do occur, they tend to be missed because the patient is not investigated during an attack.] *Denys Jennings*

2548. **Ulcerative Colitis in Children.** [In English]
R. LAGERCRANTZ. *Acta Paediatrica* [*Acta paediatr., Stockh.*] Suppl. 75, 89–151, 1949. 2 figs., bibliography.

After reviewing the literature on ulcerative colitis, the author gives a detailed analysis of 134 personal cases (78 in boys and 56 in girls). As in other series no guide to aetiology was found. The disease is becoming commoner in Stockholm, and the author says that psychological factors may have some connexion with this.

In general the findings of case analysis and follow-up study are similar to those of other authors, and the prolonged course of the disease, with remissions and relapses, is stressed. Not until after a period of 2 years without a relapse can a cure be considered to have been effected.

N. M. Jacoby

2549. **Acute Intussusception in Infants and Children.** (L'invaginazione acuta nel lattante e nel bambino)
V. ZAFFAGNINI and G. NIERO. *Clinica Pediatrica* [*Clin. pediat., Bologna*] **31**, 321–354, June, 1949. 9 figs., 43 refs.

Intussusception in infants and young children appears to be commoner in Great Britain, Australia, Denmark, and North America, than in other countries. This report concerns 35 cases treated during the 10 years 1938–48 in Bologna, of which 24 were in children under the age of one year. Most of the patients were between 4 and 5 months old, the youngest being 3 months and the oldest 11 years. There were 27 males and 8 females. Two patients had had mucous diarrhoea 24 hours before the main attack, a few others had had such an attack several weeks previously, and 2 had had fever and one bronchitis for a few days previously. Otherwise there were no prodromal symptoms. The main attack was ushered in with pain in all but one instance, and the pain was usually followed by vomiting and/or bleeding within the

next 24 hours. The pain was of the usual type—spasmodic and intense, with flexing of the thighs, and followed by pallor. It lasted for several minutes with 5- to 15-minute intervals. The patients were quiet in the intervals and sometimes went to sleep. Vomiting was projectile at first and abundant. Later it became regurgitant and faeculent. Rectal bleeding was considered pathognomonic, and was present in the first 12 hours in 14 cases. It usually disappeared after 24 hours, and in 6 cases it was absent up to the time of operation.

The infants were in a normal state of nutrition on admission and their general appearance between spasms was good but in the later stages dehydration was obvious. The temperature was normal in the first 24 hours, and the pulse rate was always disproportionately raised. An abdominal tumour was palpable in 25 cases. Of the 16 patients seen in the first 24 hours, a lump was found in only 10. It was often not palpable at a second examination. Distension was present in 20 cases, and visible peristalsis, seen only during the spasms of pain, in 8. The authors cast doubt upon the value of Dance's sign (emptiness in the right iliac fossa). The apex of the intussusception was palpable per rectum in 4 cases, and in most of the others blood was found on the examining finger. *X*-ray examination, either plain or with a barium enema, was found to be of little value in diagnosis.

In 8 cases reduction was attempted by means of a barium enema, administered without manipulation to healthy babies in the first 24 hours. Reduction was complete in 2 cases and partial in 4, as checked by repeated *x*-ray films. In the successful cases, films were again taken after another 24 hours. Operation was performed in the 6 cases in which the enema failed, and in all the others. The authors maintain that the enema had made the operation somewhat easier. A simple reduction was performed and no resection was carried out unless it was genuinely indicated by the state of the bowel after reduction. In fact, resection was carried out in only one case, which ended fatally. There were 11 deaths altogether, all of patients first seen after the first 24 hours. The parenteral administration of fluids is stressed [but there is no mention of the type of anaesthetic used]. *Tom Rowntree*

2550. **Acute Intussusception in Angioneurotic Oedema.** (Edema di Quincke ed invaginazione intestinale)
P. MARINELLI. *Clinica Pediatrica* [*Clin. pediat., Bologna*] **31**, 355–366, June, 1949. 35 refs.

A previously healthy boy, 6 years old, was admitted to hospital with a history that 18 days previously he had had a sudden swelling of the lower third of the left leg and at the same time complained of cramp-like abdominal pain. These two symptoms lasted 2 days and subsided as quickly as they came. Three days later the upper lip swelled and this was again associated with abdominal pain. This time the symptoms lasted only for a few hours. Then the scrotum swelled. Three days before admission the abdominal pain returned and he passed some mucus from the rectum. He next developed complete obstruction. On admission he looked ill, and the abdomen was distended and tympanitic. Rectal examination showed no abnormality, but it was only possible to examine the abdomen adequately under an anaesthetic, when a sausage-shaped tumour was felt in the right lower quadrant and the diagnosis of intussusception was made. Laparotomy revealed the intussusception to be ileo-ileal and reducible, but it was necessary to resect the apex and to make an end-to-end entero-anastomosis. The patient made an uninterrupted recovery.

The case is reported as illustrating an unusual cause of intussusception and an unusual manifestation of angioneurotic oedema. An extensive review of the literature follows. *Tom Rowntree*

2551. **Recurrent Small Intestinal Intussusception in Children**
M. D. TEITELBAUM and N. ARENSON. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 80–88, Jan., 1950. 11 figs., 9 refs.

Five cases of intussusception of the small intestine in children are described, 4 being illustrated by radiographs. The condition is apparently more common than is generally assumed. It is probably a neuromuscular disorder and in some instances may be an allergic manifestation. The intussusception, which is transient and recurrent, usually involves multiple segments of the small intestine and in most cases causes intermittent abdominal pain with nausea, and sometimes with vomiting. The symptoms may be present for months or years and the attacks may be very severe. However, there is no strangulation or obstruction. No tumour mass can be felt and intestinal haemorrhage does not occur.
A. Orley

See also Section *Radiology*, Abstract 2487.

2552. **The Treatment of Acute Leucemias of Childhood with Folic Acid Antagonists**
E. J. WEBER, F. E. KARPINSKI, and R. W. HEINLE. *Journal of Pediatrics* [*J. Pediat.*] **36**, 69–78, Jan., 1950. 1 fig., 9 refs.

Folic acid antagonists produced temporary symptomatic and haematological remissions of leukaemia in 20 of a group of 24 children studied at Cleveland, Ohio. The diagnosis in all cases was based upon clinical findings and bone-marrow studies.

"Aminopterin" (4-aminopteroylglutamic acid), 1 mg., was given intramuscularly daily at the onset of treatment and then every other day until toxic effects were observed. Toxic reactions included ulceration of the mouth, fever, and anaemia. The individual response varied but the main effects were: (1) Depression of the bone marrow with reduction in the normal and abnormal elements, associated with anaemia and leucopenia in the peripheral blood, and bleeding resulting from a lowered platelet count. (2) Recovery of marrow cellularity after the drug had been discontinued, with an almost normal peripheral blood picture in several patients. (3) Gradually increasing numbers of abnormal cells in spite of further treatment. (4) Aplastic anaemia with severe hypoplasia of the marrow at necropsy.

Three patients died within a few days of admission and the action of the drug could not be assessed. In 8 patients there was severe initial bone-marrow depression, and haemorrhagic phenomena contributed to an early death. In 4 there was a moderate haematological response but marked clinical improvement. In 9 there was symptomatic improvement with absence of abnormal cells for several weeks. In these cases the survival time was prolonged and was 48 weeks in one instance. At necropsy in 5 cases there was little if any evidence of leukaemia, the bone marrow being fibrotic and acellular.

The mechanism of action of the drug is discussed and the authors conclude that deprivation of folic acid disturbs the cell enzyme systems, this action being more marked in the case of leukaemic cells because of their rapid metabolic processes. Failure of the acute leukaemias to respond as satisfactorily as chronic leukaemias is attributed to the small difference between metabolic requirements of normal and abnormal cells in acute leukaemia. *R. M. Todd*

2553. **Mongolism and Heredity.** (Mongolisme og arvelighed)
G. V. BREDMOSE. *Nordisk Medicin* [*Nord. Med.*] **42**, 1923–1925, Dec. 12, 1949. 4 refs.

The author has gathered all the available information about the relatives of 51 mongols, 51 idiots, 51 imbeciles, and 51 feeble-minded persons. All the facts concerning the last 3 categories were obtained from institutions for comparison with the author's data on his own series of mongols. The survey showed that mental deficiency was present in 3·7% of relatives of mongols, 6·5% of those of idiots, 11·2% of those of imbeciles, and 7·6% of those of the feeble-minded. Personality defects (psychoses or neuroses) were equally common in all 4 groups, but the incidence of epilepsy among the mongol families (0·8%) was only half of that in the other groups. Deaf-mutism was about 5 times and stillbirth about 4 times as common among the mongol families as in the other groups.
B. Nordin

2554. **Subdural Hematoma and Effusion in Infants. Review of Fifty-five Cases**
A. R. ELVIDGE and I. J. JACKSON. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **78**, 635–658, Nov., 1949. 10 figs., 24 refs.

In a review of 55 infants with subdural haematoma and effusion, the cases are divided as follows: (1) Definite birth injuries (10 infants). Difficult labour, spasticity, tense fontanelle, seizures, respiratory difficulties, and opisthotonus were the chief clinical features. Treatment was by elevation of depressed fractures, trepanation, and drainage, or by craniotomy and evacuation of fluid. Six died. In 9 cases the subdural fluid was bloody; in only 1 was blood clot seen. Bilateral effusions were present in 8. Two survivors of trepanation were normal 9 and 10 years later respectively. One infant who underwent craniotomy was mentally retarded at 1 year. (2) Probable birth injuries (26 infants aged 13 days to 14 months, with histories of difficult labour or congenital symptoms). All had hydrocephalus and convulsions. Spasticity, reluctance to feed, and respiratory difficulties were common symptoms. Physical signs were various and of no localizing value. Otitis was present in 6. Treatment consisted of subdural aspiration, trepanation, and craniotomy if necessary. Bilateral effusions were present in 19 cases. The fluid was xanthochromic in 18, bloody in 8. Blood clots within the effusion were seen only in 4 cases. The spinal fluid was normal in 7 patients, yellow with increased protein in 2, and bloody in one 15-day-old baby. Five died after operation. Of 14 infants followed up for 6 months to 6 years, half were normal. (3) Postnatal head injuries (9 patients aged from 2 to 30 months). Six unconscious patients were operated on soon after admission, and all died. Of 3 patients admitted 2 to 6 weeks after injury, 1 was practically normal 2 years after trepanation, and 1 died. (4) Unclassified (10 infants, aged 2 to 24 months). Chronically ill patients, with unsatisfactory histories. Hydrocephalus, seizures, and paresis were the commonest symptoms. Six had extracranial infection, usually otitis. There was a bilateral effusion in 7 and a subdural membrane in 4. Cerebrospinal fluid was usually normal. Two patients died. Four were followed up for 1 to 3 years and 3 were normal. (One died from congenital heart disease.)

Any infant with hydrocephalus and seizures should be suspected of having a subdural effusion. Diagnosis is made by puncture at the lateral angles of the fontanelle with a short No. 18 lumbar-puncture needle inserted obliquely. Puncture posteriorly through the lambdoid suture may be desirable in some very young infants. Aspiration should not be used. *X*-rays may reveal fracture or separation of sutures. Pneumography is useful in diagnosis, when a fluid level in the brow-up or brow-down position may be shown, to estimate the amount of residue after operation, to determine a shift of midline structures, or to follow the degree of ventricular dilatation or cerebral atrophy. Ventriculography through the anterior fontanelle is the method of choice except in very small infants.

Treatment may be by (1) repeated subdural aspiration, which is useful in acute cases and is especially suitable for the newly born; (2) trepanation, indicated if the brain has not expanded and pressure remains high, and especially for identification of a membrane—in the absence of which the subdural space must be drained for 1 to 5 days; (3) craniotomy, in cases where an inner membrane is found; operation is performed on the same day as trepanation, the membrane is completely removed, and sometimes a small quantity of modified Ringer's solution is injected by lumbar puncture to aid brain expansion; (4) continuous closed drainage, in which negative pressure makes rapid closure of the subdural space possible, but which is a dangerous procedure. As repeated removal of fluid from the subdural space entails the loss of as much as 5% of the patient's daily need of protein and 10 to 20% of his daily fluid requirements, intravenous infusions of blood, plasma, and glucose–saline are necessary in the acute stage, and high-protein feeding is indicated during convalescence.
J. Vernon Braithwaite

2555. **The Treatment of Diabetes in Childhood**
A. LICHTENSTEIN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **24**, 237–244, Dec., 1949. 4 figs.

The author urges that diabetes in childhood should be stabilized by means of insulin without dieting. He points out that there is ample evidence for the fact that the diabetic requires a normal balanced diet. In addition, he emphasizes that authorities vary greatly in their dietetic specifications, and that the average of their recommendations differs little from the diet taken when no restrictions are imposed. The author has used " free diet " treatment consistently since 1933. The child has as much freedom in diet, including sugar and sweets, as a normal Swedish child living in conditions where a normal diet is balanced.

Each child entering hospital is kept on ordinary diet and the diabetes is controlled by insulin. Control, which is usually established within a week, means a sense of well-being, normal appetite and thirst and urinary output, freedom from subjective symptoms, and absence of ketonuria. Glycosuria of moderate degree does not matter, and the fasting blood sugar level usually varies between 100 and 200 mg. per 100 ml., this relative hyperglycaemia having no ill effects. Children on this treatment, compared with those on a low-carbohydrate diet, show a greater resistance to acute infection and tuberculosis, and a lower frequency of coma and hypoglycaemic attacks. They grow and develop normally.

The important long-term complication of diabetes is cardiovascular disease. The free-diet technique has only been in use for 15 years and so it is not yet possible to publish truly comparable results, but of 50 cases after 12 years 30% showed albuminuria, 30% hypertension, 12% calcified arteries, and 60% retinal haemorrhages. These figures appear no worse than those in reports from other sources. Similarly a mortality rate of 6% for free-diet cases after 15 years is no higher than the rates with restrictive diets.

The type of insulin most suitable for use will vary from patient to patient, but the author finds that Hagedorn's protamine insulin is usually best. Zinc protamine insulin is less suitable for children. A large-scale comparison of dosage for all ages in Sweden revealed the need for an average of 52 units daily in cases treated with restrictive diets as against 56 units for those on free diets, an insignificant difference.

The author emphasizes that psychological results from the free-diet treatment in children are good, as well as the physical.

[This is a very stimulating article, but unfortunately records are not quoted in sufficient detail to substantiate all claims.] *E. H. Johnson*

2556. **Studies in Coeliac Disease. Fat Absorption**
W. SHELDON and A. MACMAHON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **24**, 245–249, Dec., 1949. 5 figs., 8 refs.

The authors report three investigations on fat absorption in coeliac disease and other forms of steatorrhoea. The first study is a continuation of Sheldon's work on the inverse relation of fat absorption in coeliac disease to starch intake. In 4 cases fat balance was determined while the child was on a starch-free diet containing 20% of the carbohydrate as dextrin, and then while it was receiving 50% dextrin, the starch having been replaced by the first product of its digestion. The results showed that the percentage of fat absorbed falls when extra dextrin is added, in the same way as it does when starch is given.

The second investigation was of the relation of starch intake to fat absorption in other forms of steatorrhoea. In 4 children with fibrocystic disease of the pancreas fat balance was determined with and without starch in the diet. Fat absorption was lower than in coeliac disease, and the presence or absence of starch made no difference.

The third investigation was of the chylomicron curve in coeliac disease. Frazer has shown that a proportion of fat in the diet is emulsified in the small intestine, and absorbed as fat into the lacteals, whence it enters the systemic circulation. The number of droplets per field were counted at half-hourly intervals after a meal of fat, and recorded graphically. Results showed that in children with coeliac disease absorption of fat by this route is impaired. The authors also confirmed that the duodenal content of lipase in coeliac disease is normal. In a further group of 8 children whose clinical state was steadily improving while they were receiving a starch-free diet, the chylomicron curves were almost normal. This curve was not affected by a starch meal; the curve is influenced by the state of the disease, and not by the composition of the immediately preceding meal.

E. H. Johnson

2557. **Coeliac Disease and the Coeliac Syndrome**
G. E. M. SCOTT. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 37–46, Jan. 14, 1950. 14 figs., 49 refs.

A general discussion of the syndrome of steatorrhoea, malnutrition, and abdominal distension is given. The author then describes the results of the examination of necropsy material from 16 microscopically proven cases of fibrocystic disease of the pancreas, previously treated at the Children's Hospital, Melbourne, between the years 1945 and 1948. Half of these patients (5 females and 3 males) had died before the age of 12 months. Of the 8 who lived for more than 12 months, 7 were females and only one a male. Microscopical examination of the pancreas revealed varying degrees of fibrosis—sometimes enclosing spaces filled with erythrocytes—round-cell infiltration, atrophic acini which had sometimes ruptured and coalesced, metaplasia of the duct epithelium, and sometimes large spaces lined by epithelium which varied in form from the flattened to the columnar. The liver was on occasion the seat of biliary cirrhosis or patchy fatty changes and fibrosis with cellular infiltration. In one case section of the liver merely revealed extensive haemorrhage and small-cell infiltration without any trace of liver tissue. The submucosa of the trachea sometimes showed a massive cellular infiltration. The pulmonary changes were of the nature of purulent bronchitis, and no example of cystic disease of the lung was encountered.

I. H. Milner

Medicine: General

2558. **Value of Southey–Leech Tubes in Rapid Relief of Massive Edema**
M. J. Fiese and J. M. Thayer. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 132–143, Jan., 1950. 20 refs.

Mechanical removal of oedema fluid is a sound physiological procedure. The Leech modification of the Southey tube permits greater drainage than any other model. The prophylactic use of penicillin has abolished the risk of infection. The authors describe results in 16 cases of refractory or massive oedema due to nephritis, heart failure, generalized lymphosarcomatosis, and constrictive pericarditis. Use of the Southey–Leech tube is contraindicated in infected, hard, or brawny oedema.
Alan Kekwick

2559. **Effects of Bed Rest on Cardiovascular Function and Work Performance**
H. L. Taylor, A. Henschel, J. Brozek, and A. Keys. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 223–239, Nov., 1949. 3 figs., 28 refs.

Six healthy young men whose ages were from 20 to 33 years were studied before, during, and after a 3- to 4-week period of bed rest. Measurements were made under rigidly controlled conditions on the performance of the cardiovascular system (at rest, in the upright posture, and during work), and on speed, coordination, and strength. A high degree of conditioning for the performance of all tests was achieved before the bed rest period.

Bed rest produced a 17% decrease in heart volume and an 8% decrease in the transverse diameter of the heart. There was a highly significant increase in the resting pulse rate, which averaged 0·5 beats per minute for each day of bed rest. The pulse rate at the end of a half-hour walk at 3·5 miles [5·6 km.] per hour and 10% grade increased by 40 beats per minute after bed rest. There was no change in the mechanical efficiency during this walk, as the result of bed rest. The oxygen intake during a 90-second run at 7 miles [11·26 km.] per hour and 15% grade was reduced by 730 cc. of oxygen or 16% after 3 to 4 weeks of bed rest. This was accompanied by increases in oxygen debt and blood lactate after the run and a decrease in mechanical efficiency. The maximal oxygen intake was determined in 2 men who showed decreases of 13 and 22% after bed rest. Bed rest produced a marked deterioration in the cardiovascular response to posture as measured by pulse rate and blood pressure changes produced by tilting to 68° on a tilt table. Ataxiameter studies showed that a definite increase in sway resulted from bed rest. Coordination, as measured by pattern tracing, suffered a small loss as the result of bed rest while speed of small hand movements, of medium arm and hand movements, and of gross body and arm movements showed no deterioration. Grip strength was not influenced by bed rest and back strength showed only a small deterioration.

After bed rest the rate of recovery of the various functions was roughly proportional to the extent of the deterioration in bed rest. Strength, coordination, and postural sway recovered early (4 days); blood lactate after exhausting work, and the oxygen cost of exhausting work recovered at an intermediate time (2 weeks); pulse rate during grade walking and O_2 intake during exhausting work recovered late (between 2 and 5 weeks), and the cardiovascular response to posture was very late in returning to normal (after 7 weeks). In one man the effect on the principal components of fitness of a herniorrhaphy with bed rest for 3 weeks was of the same order of magnitude as bed rest alone.

It is concluded that the deconditioning due to bed rest has special characteristics, with the major loss of performance occurring in the cardiovascular system.—[Authors' summary.]

2560. **Studies on the Mechanism of Cardiac Injury in Experimental Hypothermia**
K. Lange, D. Weiner, and M. M. A. Gold. *Annals of Internal Medicine* [*Ann. intern. Med.*] **31**, 989–1002, Dec., 1949. 8 figs., 13 refs.

Electrocardiographic changes were detected in rabbits exposed to a temperature of −20° C. There were pronounced changes in the ST segments and in the T waves, prolongation of the P–R interval, and slowing of the heart rate. The alterations in the P–R interval and in the heart rate were directly proportional to the fall in body temperature. Furthermore, the QRS complex was found to be prolonged approximately in proportion to the fall in temperature. In order to produce an increase in oxygen dissociation, the blood was acidified by means of intravenous injections of acid sodium phosphate. As a result, the ST segments and the T waves became normal, but the P–R interval was prolonged and the rate of the heart continued to decrease. The ST segments and the T waves also became normal when the amount of oxygen in the plasma was increased by placing the animals in a compression chamber and exposing them to an atmosphere of oxygen under a pressure of 75 lb. per square inch (12·3 kg. per sq. cm.).

It was concluded, therefore, that the heart had been damaged during the state of anoxia. Anoxaemia was not a factor in the pathogenesis of the condition, for artificial respiration with pure oxygen failed either to prevent or to alter the electrocardiographic manifestations produced by hypothermia. During the course of the investigation a prolongation of systole was discovered. The phenomenon was attributed not only to anoxia but also to the direct effect of cold on the cardiac muscle fibres. The possibility arises that when death occurs after exposure to severe cold, the cause is attributable to the adverse

effects of anoxia upon the heart muscle. From the therapeutic point of view, the indication is to treat patients recovering from hypothermia as if they had a transient myocardial infarction. *A. Garland*

2561. **The Pathogenesis and Treatment of Iron Deficiency Conditions With Little or No Anaemia.** (Ueber Pathogenese und Therapie der nicht-anämischen und leichtanämischen Eisenmangelzustände)
B. Jasiński. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 1255–1266, Dec. 31, 1949. 1 fig., 14 refs.

The author has previously shown that iron absorption, as judged by the rise in serum iron level after a single test dose of ferrous gluconate, is much greater in the iron-deficient patient than in those with adequate iron supplies. Using this test, he studied a group of 26 persons suffering from mild anaemia with haemoglobin values between 62 and 96%. Only 4 males were included, these being all below 20 years of age. Initial fasting serum iron values were low in all except 2 cases, ranging from 8 to 92 μg. per 100 ml. and being above 100 μg. per 100 ml. in the remaining two.

Following oral ingestion of the test dose of iron the serum iron level rose to a maximum at about 10 hours, the peak figure varying from 194 to 490 μg. per 100 ml. (normal max. 280 μg.). In 10 cases absorption curves were again studied during the course of iron therapy. In all the fasting level of iron in serum rose and the peak at 10 hours became progressively lower, indicating a diminished absorption. It is found that iron deficiency, as judged by the iron-absorption curve, may be present in spite of normal haemoglobin value and erythrocyte count. The author considers indeed that it may be of frequent occurrence. Finger-nail changes and other clinical signs of iron deficiency are lacking, being late developments. The minimal period for complete recovery under iron therapy is estimated to be 6 weeks, 3 to 4 months being required in manifest anaemia. [The validity of the claim that a pre-anaemic stage of iron deficiency exists rests on the reliability of the absorption curve as an indicator of such deficiency.]
C. L. Cope

2562. **Acute Idiopathic Porphyria Presenting as a Progressive Paresis of Landry Type**
F. D. Hart and P. Collard. *British Medical Journal* [*Brit. med. J.*] **1**, 278–279, Feb. 4, 1950. 2 figs., 7 refs.

The case is described of a woman aged 45 who had a subtotal hysterectomy and bilateral salpingo-oophorectomy with removal of a chocolate cyst. Fifteen days after operation (July 2) she complained of malaise and weakness, and 3 days later had flaccid weakness of the legs with retention overflow and mental dullness. By July 7 the weakness of the legs had increased and the arms were also affected. On July 10 the diaphragm movements became paradoxical. Mental confusion, slurred speech, and rapid respiration were noted, together with the following physical signs: no pupillary reaction to accommodation, bilateral absence of corneal reflexes, left lower facial paralysis, a flaccid tetraparesis, most severe in the legs, weakness of the trunk muscles, complete absence of all deep reflexes, absence of abdominal reflexes, and ill-defined areas of anaesthesia over both legs.

The urine was almost normal in colour but darkened on heating. Waldenstrom's test for porphobilinogen was strongly positive and total porphyrin concentration was 25 mg. per litre, mainly consisting of uroporphyrin of unknown type. The cerebrospinal fluid contained no cells and globulin content was not increased. The patient died on July 11, 10 days from the first onset of symptoms.

Necropsy revealed a purple-brown coloration of the heart muscle, black pigment scattered over the peritoneum, and a definite pressure cone. The authors give the histological findings, which agree with those described previously. There was no history of any previous attack nor was there any known drug idiosyncrasy. Potassium citrate, sulphadiazine, and an occasional dose of phenobarbitone had been given in the post-operative period. The authors point out that unless examination of the urine had revealed uroporphyrin the diagnosis might have been missed. In their view it is more likely that this was a case of acute idiopathic porphyria than a case of toxic porphyria. *K. Black*

2563. **Effects of Dietary Depletion of Riboflavin**
M. K. Horwitt, O. W. Hills, C. C. Harvey, E. Liebert, and D. L. Steinberg. *Journal of Nutrition* [*J. Nutrit.*] **39**, 357–373, Nov. 10, 1949. 1 fig., 20 refs.

The subjects of this study were 15 male patients in a mental hospital, with 14 similar subjects as controls. They were given a 2,200-Calorie diet containing 0·55 mg. of riboflavin daily. The equivalent diet in rats resulted in retarded growth and a great diminution in the rate of healing of experimentally inflicted wounds. The human subjects on the restricted diets developed signs of deficiency, beginning in one subject after 4 months, which included angular stomatitis, seborrhoeic dermatitis, lesions of the scrotal skin, and a decrease in flicker-fusion frequency. The type of abnormality found seemed to be related to the trauma, irritation, or infection to which the tissues were subjected. There was no change in the level of pyruvic or lactic acid in the blood. The amount of the vitamin in the urine tended to remain constant with intakes up to 1·1 mg. daily, so that it appears that an adequate level of riboflavin cannot be maintained when the daily intake falls below this figure. *J. Yudkin*

DIABETES

2564. **Mechanism of Cutaneous Reactions to Insulin**
R. G. Paley. *Lancet* [*Lancet*] **2**, 1216–1218, Dec. 31, 1949. 2 figs., 21 refs.

The author reviews the literature on local sensitization to insulin and draws attention to the original paper by Banting, who attributed cutaneous insulin reactions to protein impurities in the insulin. The recorded incidence of reactions varies from 7·5% to 30%. In the present series of 147 cases studied at the General Infirmary, Leeds, reactions occurred in 55·8% of patients. There

were mild reactions in 81·7% and severe reactions in 18·3% of the " reactor " group.

For studying the mechanism of reaction the method used was to inject intracutaneously: (1) water at *p*H 3 to 3·2; (2) the same with 0·3% cresol; (3) ordinary soluble insulin; (4) buffer solution at *p*H 7 to 7·2; (5) sterile 1% solution of salmine sulphate at *p*H 3 to 3·2; (6) commerical zinc protamine insulin. The tests were made on the flexor surface of the forearm with separate autoclaved tuberculin syringes, and the reactions read in 15 minutes. In 34 diabetic patients who reacted to various brands of insulin, recrystallized insulin which had been repurified six times was used for intracutaneous injection. The results obtained indicate a great quantitative diminution in the area of reaction if recrystallized insulin is used; this confirms the work of Jorpes in Sweden.

The author also records 2 cases in which the area of reaction to an intracutaneous injection of recrystallized insulin approximated to that caused by commercial insulin. It is suggested that in some cases the patient may be sensitive to insulin protein itself. However, in most cases of cutaneous sensitivity to commercial insulin the author suggests the use of recrystallized insulin.

I. McLean-Baird

2565. **Electrolyte Balance in Uncontrolled and Controlled Diabetic Ketosis and Acidosis**

J. Weissberg, T. H. McGavack, A. M. Shearman, and I. J. Drekter. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **9**, 1259–1272, Dec., 1949. 4 figs., 26 refs.

Cases of diabetic coma have been reported in which the hyperglycaemia, acidosis, and ketosis responded to treatment with insulin and fluids, but in which the patient continued to show alarming symptoms or died. These deaths may be due to vascular or cardiac failure but some may be caused by unrecognized yet profound changes in electrolyte balance.

Five patients were admitted to hospital with severe diabetic ketosis and acidosis (two of them in coma), and ketosis was induced in eight diabetics by reducing or stopping their insulin; all were treated in the usual manner with insulin and fluids, and their blood electrolyte levels and electrolyte balance were studied. The balance studies were facilitated by the use of a liquid diet.

The serum potassium level fell in all the patients at some point during insulin treatment. Some of the falls were to dangerous levels (2 to 3 milliequivalents per litre) and in 2 cases were accompanied by weakness and hypotonia; one of these patients was given Darrow's solution with benefit. The fall in serum potassium level ran parallel with the fall in blood sugar level, but the absolute values were unrelated. Fluid balance showed that dilution of extracellular fluid was insufficient to account for the result, and this was also borne out by the fact that serum sodium and chloride levels were either unaltered or showed changes opposed to those of serum potassium levels. The changes in serum phosphate level were similar to the changes in serum potassium.

The patients in whom ketosis was induced and whose electrolyte balance was known during its onset and treatment had negative potassium, sodium, and chloride balances until insulin was given, and positive balances afterwards. Thus the potassium lost from the serum is not excreted and must be concentrated somewhere in the body unless it has undergone some chemical combination making it undetectable by the usual method. No doubt potassium has been lost from the body during the diabetic diuresis and this depletion presumably allows deficiency to develop despite a positive balance.

The maximum fall in serum potassium level is found 18 to 42 hours after the start of insulin treatment and occurs whether ketosis or acidosis is the cardinal symptom. The symptoms of potassium deficiency are like the symptoms of diabetic ketosis with coma; if these continue in spite of a satisfactory blood-sugar response to insulin, potassium deficiency must be suspected. Its symptoms occur in this order: restlessness, general hypotonia, apathy with loss of deep tendon reflexes, paralysis of the diaphragm, respiratory embarrassment, and anoxaemia. The serum potassium level is an indication, but not a measure, of potassium deficiency; symptoms develop in different individuals at different serum potassium levels.

Peter C. Williams

2566. **Diabetic Glomerulosclerosis**

J. W. Harman. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6**, 28–33, Jan., 1950. 1 fig., 17 refs.

In an analysis of the necropsy findings in 116 cases of diabetes the author adds further confirmation of the specificity of the " intercapillary glomerulosclerosis " described by Kimmelstiel and Wilson, but fails to establish criteria for its diagnosis in life. In no instance was the characteristic glomerular lesion seen in the absence of arteriolosclerosis, and arteriolosclerosis involving the efferent glomerular vessel is claimed as being as specific to diabetes as is the intercapillary glomerulosclerosis.

G. M. Bull

5267. **A Case of Coexisting Insulin Allergy and Insulin Resistance**

W. B. Sherman. *Journal of Allergy* [*J. Allergy*] **21**, 49–54, Jan., 1950. 20 refs.

A patient admitted to the Presbyterian Hospital, New York, in diabetic pre-coma was given between 1,000 and 1,600 units of insulin per day for the first 4 days, this dosage then being reduced until, after 10 days, the amount of insulin required daily varied between 85 and 180 units, stabilization being very difficult. An urticarial reaction at the site of the injection occurred when standard insulin was given and also after the injection of crystalline insulin from beef and pork sources, but was satisfactorily controlled by 50 mg. of " pyribenzamine " given 3-hourly. During the first month of treatment the patient's serum was found to contain a factor which neutralized the hormonal activity in mice of beef and pork insulin, but not of human insulin. This factor was not destroyed by heating to 56° C., but the serum contained also a skin-sensitizing antibody which was destroyed at this temperature. This

antibody also reacted only with beef and pork insulin. No antibody blocking the allergenic activity of insulin could be detected, but this may have been due to technical reasons. Precipitin tests with serum and crystalline insulin gave negative results. The concentration of neutralizing and skin-sensitizing factors in the serum decreased as the patient's condition improved and the demand for insulin fell. *H. Herxheimer*

ALLERGIC DISORDERS

2568. **Preliminary Report on Adrenocorticotrophic Hormone (ACTH) in Asthma**
B. Rose, J. A. P. Pare, K. Pump, and R. L. Stanford. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **62**, 6–9, Jan., 1950. 20 refs.

It is known that there is a correlation between the adrenal cortex and histamine metabolism. It has also been shown that adrenocorticotrophic hormone (ACTH) causes a reduction in number of circulating eosinophils. Six severe chronic asthmatics, one of whom had rheumatoid arthritis and another periarteritis nodosa, were treated with ACTH. Intramuscular injections were given at 6-hourly intervals. Two patients received 150 mg. daily for 2 days and then 100 mg. for 2 more days. The next 4 patients received 100 mg. daily for 3 days, 75 mg. daily for 2 days, and 25 mg. on the last day. Four patients showed complete remission of all signs and symptoms within 48 hours, the remaining two being markedly improved. It was also found that histamine or " mecholyl " no longer depressed respiratory function in 4 patients. The immediate type of skin-test reaction was, however, not altered. In 5 cases there was marked or complete disappearance of histamine from the urine and in all cases there was an increase in urinary histidine content. There was marked associated improvement in the arthritic and periarteritic signs and symptoms. In 1 case of asthma relapse was complete after 6 weeks.

[For those interested the paper should be consulted in the original, together with a similar communication by Bordley *et al.*, *Bull. Johns Hopk. Hosp.*, 1949, **85**, 396.]
A. W. Frankland

2569. **Significance of Mediastinal Shift in Asthma**
L. H. Osmond. *Annals of Allergy* [*Ann. Allergy*] **7**, 799–806, Nov.–Dec., 1949. 6 figs., 8 refs.

Mediastinal displacement is commonly observed in the asthmatic state. The possible mechanisms leading to collapse or emphysema of one or more pulmonary segments, with consequent mediastinal shift, are discussed. On radiological examination, even minor degrees of displacement may be detected by screening or by comparison of radiographs taken in complete inspiration and complete expiration. Transient changes probably arise from the presence of a mucous plug in a bronchus. More permanent signs may be caused by narrowing of the bronchus as a result of oedema of the mucous membrane (often associated with a mucous plug acting as a ball valve either above or below the obstruction) or by inflammatory bronchostenosis.

In persistent cases bronchoscopy should be undertaken, and may enable a mucous obstruction to be removed or dilatation of a bronchostenosis to be carried out. The latter condition is often accompanied by a severe persistent cough, often non-productive until a sudden profuse expectoration of sputum occurs. Recurrent febrile episodes are common and are usually associated with the finding of an area of reduced breath sounds on auscultation of the chest. Adequate treatment at an early stage is important and may prevent the further development of the stenosis before it has become irreversible.
R. S. Bruce Pearson

2570. **Emotional Conflict and Allergy**
T. M. French. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **1**, 28–40, 1950. 11 refs.

The author presents an essay on the relationship between emotional tension and allergic states, with many quotations from the literature. Illustrations are drawn mainly from studies upon asthma, and an attempt is made to answer some of the questions which have arisen from these studies. One question, for example, is how far the anxiety and sense of insecurity of many asthmatic children are the outcome of difficulties produced by the disease itself. It was shown by Rogerson and his associates (*Guy's Hosp. Rep.*, 1935, **85**, 289), that appropriate psychological treatment of both mother and child was followed by diminution in frequency and severity of asthmatic attacks. The inference was that the anxiety which these children showed before treatment was a contributory cause of the asthma. A description of the " asthma–prurigo personality " was given by these workers—high intelligence on verbal testing, but with a poorer performance ability; marked over-anxiety and lack of self-confidence; and considerable latent aggressiveness and egocentricity. Further evidence is provided by Wittkower (*J. ment. Sci.*, 1935, **81**, 533), who showed that whereas a demonstrable cutaneous allergy can neither be produced by suggestion, nor removed by it, the asthma-producing effect of an allergen can be inhibited, without change in the allergic state of the skin, by suggestion.

Some evidence of the nature of the " focal conflict " associated with asthmatic attacks was found by the author and Alexander (*N.R.C. Psychosomatic Medicine Monograph IV*, Washington, D.C., 1941), who also were successful in relieving symptoms by means of psychotherapy in many cases of asthma and concluded that it was likely that the undercurrent of dependence so common among these patients was an aetiological factor in the condition and not a secondary effect. It was noted that when, during the course of psychoanalytic treatment, fears of separation from a " mother-figure " were mobilized the attacks would increase; attacks also tended to occur at week-ends, or when the analysis was interrupted. One conclusion which emerged from this study was that emotional and allergic factors stand in a complementary relation to one another. In some patients attacks are precipitated by emotional tension alone, in some only by an allergic reaction, and in other cases both elements may be necessary.
Desmond O'Neill

2571. **Allergy and Emotions. A Review**
M. L. MILLER. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **1**, 40–50, 1950. Bibliography.

In a review of the literature relating to the psychosomatic approach to allergic disorders, the authors give a bibliography of 70 references, a few only of the principal findings being outlined here. Alexander and French (*N.R.C. Psychosomatic Medicine Monograph IV*, Washington, D.C., 1941) outlined the investigation and treatment of 27 asthmatic patients by psychoanalytical methods. It was concluded that, in general, attacks of asthma tended to be produced by situations which threatened to separate or estrange the patient from his mother or a mother-substitute. In these circumstances the attack seemed to have the significance of a suppressed cry. In the theme situations there was often a strong desire to make a confession to regain the mother's love; if this was successful the attack might be averted. Attacks were often precipitated by various kinds of sexual temptation. There was much variation in personality type among these patients at a superficial level, but at a deeper level they showed one common feature—an intense need for parental love and protection. Nearly all were shown to be allergically hypersensitive, but attacks during the period of analysis did not appear related to any allergen. Of 19 patients who were under treatment for 6 months or more, 9 became symptom-free, 8 were much improved, and 2 remained unchanged. Gerard (*Nerv. Child*, 1946, **5**, 327) reported the results of psychoanalytical treatment of 5 asthmatic children; after treatment all 5 remained sensitive to allergens on skin-testing, but 4 were relieved of symptoms. From the psychoanalysis of 7 patients with hay-fever, Wilson (*Psychosom. Med.*, 1941, **3**, 51) put forward the hypothesis that the psychological component in this condition is an unsuccessful olfactory repression, this being the result of unsatisfied sexual curiosity in childhood with displacement of interest to the function of elimination and the odours associated with it. Saul and Bernstein (*Psychosom. Med.*, 1941, **3**, 349) stated that the central feature in patients with urticaria was an infantile longing for love, and that when this longing is intensified and frustrated allergic sensitivity increases and symptoms appear. Emotional tension has been observed to be a precipitant of attacks of neurodermatitis by many investigators.

Desmond O'Neill

2572. **Comparative Toxicity and Side Effects of the Antihistaminic Drugs**
E. SCHWARTZ. *Annals of Allergy* [*Ann. Allergy*] **7**, 770–777, Nov.–Dec., 1949. 1 fig., 16 refs.

The toxicity and side-effects of a number of antihistaminic drugs administered in therapeutically effective doses were compared. The conditions for which treatment was given included all the commonly recognized allergic conditions. The results were as follows: (1) "Benadryl". Of 217 patients treated 133 (61·3%) complained of side-effects: in 14 cases these were sufficiently severe to necessitate stopping treatment. Drowsiness occurred in 93 cases (42·9% of the total), dryness of the mouth in 44, tingling, weakness, or burning sensation of the hands in 32, headache in 21, dizziness in 15, nervousness in 8, vomiting in 4, weakness in 2, and diarrhoea in 1. Many patients complained of more than one symptom. In addition, a number of unusual reactions were reported—mental incoordination in 3 cases and narcolepsy in 2; one patient slept for 24 hours after one dose of 50 mg., one was almost struck by a motor car twice within an hour and took refuge in hospital, and another was so drowsy while driving his car that he had to park on the road side and sleep for 2 hours. (2) "Pyribenzamine". Of 126 patients treated, side-effects were reported by 45 (35·7%). Drowsiness occurred in 17 cases (13·5%), dizziness in 8, headache in 6, nausea and nervousness in 4 each, weakness and dryness of the mouth in 3 each, and fatigue and tinnitus in 2 each. One patient, after taking 50 mg., became comatose for 6 hours, a second was so drowsy and incoordinated that he narrowly avoided an accident while driving his car, and a third developed a tachycardia of 140 per minute which lasted for 12 hours. (3) "Neoantergan". Of 141 patients treated, side-effects occurred in 35 (24·8%). Drowsiness occurred in 13 cases (9·2%), nausea and diarrhoea in 11 each, abdominal cramps in 8, headache and tachycardia in 4 each, dizziness in 3, weakness, sweating, and pruritus in 2 each, and fatigue, dry mouth, vomiting, and nervousness in 1 each. (4) "Antistin". Of 97 patients treated, side-effects were reported by 22 (22·7%). Drowsiness and nausea occurred in 6 cases each (6·2%), headache in 3, dizziness, tachycardia, and gastritis in 2 each, and diarrhoea, fatigue, nervousness, sores in the mouth, insomnia, abdominal cramps, pruritus, pharyngitis, and vomiting were encountered once each. One patient complained of a sense of constriction in the chest resembling that experienced in coronary disease, but investigations showed no evidence of cardiac abnormality and the same symptoms recurred when 100 mg. of antistin was given 2 weeks later. (5) "Histadyl". Of 89 patients treated, side-effects were reported by 18 (20%). Drowsiness occurred in 9 cases (10·1%), nausea in 3, dizziness, dryness of the mouth, abdominal cramps, and nervousness occurred twice each, and weakness, tachycardia, and fatigue once each. (6) "Neohetramine". Of 111 patients treated side-effects were reported by 8 only (7·2%). Two patients (1·2%) complained of drowsiness, and dry mouth, bitter taste, nausea, fatigue, headache, restlessness, nervousness, and aggravation of an asthmatic attack were each reported once.

The drugs were given in routine doses of 50 mg. up to four times daily, except in the case of antistin which was prescribed in doses of 100 mg., while the dose of histadyl and neohetramine was also sometimes increased to 100 mg. The author draws attention to the fact that these drugs, though useful as symptomatic remedies, are no alternative to the careful determination and elimination of aetiological factors in allergy. Serious side-effects may occur and are more common with higher dosage. Benadryl caused the most and neohetramine the fewest side-effects. However, these usually disappear if the drug is continued and it is only occasionally necessary to stop its administration.

R. S. Bruce Pearson

Cardiovascular Disorders

2573. **The Determination of Circulation Time with Lobeline.** (Sur la détermination de la vitesse circulatoire par la lobéline)
L. STANOJEVIC. *Presse Médicale* [*Pr. méd.*] **57**, 1135–1136, Dec. 10, 1949. 2 figs., 9 refs.

A method is described for the determination of the circulation time by the intravenous injection of lobeline (0·04 to 0·07 mg. per kg. body weight), the end-point being the respiratory response (gasping), which is sharp and objective in character. The average arm–lung circulation times found in a series of several hundred cases were: healthy subjects, 10·6 seconds; compensated cardiac failure, 14 seconds; decompensated cardiac failure, 30·3 seconds. [The number of cases in each group is not mentioned.] Pneumograph tracings of the respiratory changes are shown. The circulation time was shown by means of daily determinations to return to normal in a case of decompensated cardiac failure during treatment. *R. A. Gregory*

2574. **Variations in the Electrocardiogram and Phonocardiogram in Relation to the Serum Potassium Level in Hypoglycaemic Coma.** (Das Verhalten von Ekg.- und Herztonkurven, in Abhängigkeit vom Serumkaliumspiegel im hypoglykämischen Coma)
F. RUPP, W. FRITSCHY, and J. J. PAHUD. *Helvetica Medica Acta* [*Helv. med. Acta*] **16**, 324–329, Sept., 1949. 6 figs., 14 refs.

In 1948 the authors discovered that hypopotassaemia—leading to a great increase in the Q–T interval and early commencement of the second heart sound—could be produced by the administration of insulin. Simultaneous determinations of blood sugar concentration, serum potassium level, Q–T interval, and time-interval between the Q wave and the beginning of the second heart sound recorded phonocardiographically have now been carried out during insulin-shock treatment of schizophrenia [number of cases not stated]. In all cases a close relationship between hypopotassaemia and relative shortening of the interval between the Q wave and the second heart sound with respect to the Q–T interval (Hegglin's energetico-dynamic insufficiency) was observed. It is therefore recommended that the above-mentioned condition should be looked for in all cases of diabetic coma (by simultaneous registration of the electrocardiogram and phonocardiogram), in order that the threatened circulatory damage due to lowering of the serum potassium level may be recognized in time.
H. Ludwig (*Excerpta Medica*)

2575. **Normal Standards in Electrocardiograms of Healthy Infants.** (Нормативы электрокардиограммы здоровых детей раннего возраста)
M. V. RASKINA-BRAUDE. Педиатрия [*Pediatriya*] No. **6**, 43–49, Nov.–Dec., 1949.

2576. **Normal Standards in Electrocardiograms in Children of Pre-school and School Age.** (Нормальная электрокардиограмма у детей дошкольного и школьного возраста)
Z. I. EDELMAN. Педиатрия [*Pediatriya*] No. **6**, 49–57, Nov.–Dec., 1949.

2577. **The Electrocardiogram in Thyrotoxicosis: Findings Before and After Treatment with Thiouracil Derivatives.** (L'elettrocardiogramma nel morbo di Basedow—reperti E.C.G. prima e dopo trattamento con derivati tiouracilici)
M. BALDUINI and S. MAINOLI. *Folia Cardiologica* [*Folia cardiol., Milano*] **8**, 297–323, 1949. 6 figs., 42 refs.

2578. **Acute Serofibrinous Pericarditis of Undetermined Cause. A Study of Twenty-seven Cases**
R. L. LEVY and M. C. PATTERSON. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 34–45, Jan., 1950. 6 figs. 21 refs.

The authors describe 27 cases of acute pericarditis of obscure aetiology encountered during a period of 15 years. In 23 there was a history of preceding respiratory-tract infection, and it is suggested that these conditions may have been due to virus infection. In other cases the pericarditis was thought to be an allergic reaction to bacterial infection of the throat or nasal sinuses.

The course of the attack varied, but all patients recovered completely without sequelae. Follow-up examinations 6 months to 15 years later revealed no evidence of heart disease in any case. The differential diagnosis from tuberculous and rheumatic pericarditis, and from pericarditis accompanying myocardial infarction, is discussed. Electrocardiography is of assistance in distinguishing the last condition. It is noteworthy that the prolongation of the P–R interval so often seen in acute rheumatism was never observed.

Treatment with sulphonamides, penicillin, and streptomycin seemed to exert no appreciable effect on the course of the disease. The authors suggest that aureomycin treatment would be worth trying in these cases.
John Forbes

2579. **The Cardiovascular System in Toxaemias of Pregnancy.** (O aparêlho cardiovascular na toxemia da gravidez)
A. B. BENCHIMOL and R. D. CARNEIRO. *Arquivos Brasileiros de Cardiologia* [*Arch. brasil. Cardiol.*] **2**, 397–416, Dec., 1949. 9 figs., 24 refs.

The authors state that, whereas the hypertension accompanying pregnancy toxaemia has been extensively studied, the myocardial changes have not. The various theories on the aetiology of pregnancy toxaemia are reviewed. The authors maintain that 50% of hyperten-

sive women who become pregnant develop toxaemia, whereas the condition only arises in 2% of normal subjects. They also consider that the duration of the toxaemia is more important than its degree in bringing about permanent hypertension.

Cardiac asthma and acute pulmonary oedema occur in pregnancy toxaemia; the heart may become acutely dilated and later return to its normal size. They quote Dexter and White, who believe that heart failure is due primarily to the " load " of the hypertension; the modern view, however, seems to be that there is primary myocardial damage as shown by post-mortem and electrocardiographic changes. The latter, however, vary considerably, changes of left ventricular hypertrophy and even of coronary occlusion being seen in the electrocardiogram. Two cases are described, one of heart failure after the termination of pregnancy, and the other of death due to acute pulmonary oedema as a result of capillary blockage by placental cells. The latter were also found in the myocardium and the authors consider that these embolic cells may be of some significance in bringing about heart failure. *Paul B. Woolley*

2580. **Cardiac Disease in Pregnancy. A Study of the Patients With Heart Disease at the Philadelphia Lying-In Division of the Pennsylvania Hospital from 1937 to 1947, Inclusive**

J. B. VANDER VEER and P. T. KUO. *American Heart Journal* [*Amer. Heart J.*] **39**, 2–16, Jan., 1950. 50 refs.

The authors add one more to the many studies of cardiac disease in pregnancy. After discussing their findings they state that the most important problems in the diagnosis and management of patients with heart disease during pregnancy include: (*a*) the interpretation of heart murmurs in pregnancy, (*b*) the prenatal care of the patient, (*c*) the management of acute pulmonary oedema complicating pregnancy, and (*d*) the choice of anaesthetic and type of delivery. Their final conclusion is that careful prenatal observation and early control of acute respiratory infections offer most in reducing the incidence of heart failure and maternal mortality.

R. T. Grant

2581. **The Circulatory Effects of Mercurial Diuretics in Congestive Heart Failure**

L. G. C. PUGH and C. L. WYNDHAM. *Clinical Science* [*Clin. Sci.*] **8**, 11–19, 1949. 4 figs., 10 refs.

The action of mercurial diuretics on the cardiovascular system in congestive heart failure has not yet been fully studied. The authors, at the Postgraduate Medical School of London, therefore observed the effect of such drugs on right auricular pressure, cardiac output, heart rate, blood pressure, and urine output in 11 cases of congestive failure due to ischaemic, hypertensive, or rheumatic heart disease.

Right auricular pressure and cardiac output were measured by cardiac catheterization. Oxygen consumption was measured by spirometry. Right auricular pressure, cardiac output, heart rate, blood pressure, and urine volume were measured hourly for 5 to 22 hours, except in the first hour after the injection when the first two were also measured after 10 and 20 minutes. In 4 cases variations in blood volume were assessed by hourly estimation of haemoglobin level.

Four patients received 3 ml. injectio mersalylis, *B.P.*, intravenously. This contains 10% sodium mersalylate and 5% theophylline. To separate off the effects of these two drugs, 3 patients were given a freshly prepared solution of sodium mersalylate without theophylline. Since the mersalyl salt is unstable, doses equivalent to only 2 ml. of the *B.P.* preparation were given. In another 4 cases a theophylline-free preparation of a related compound, " mercuramide ", was used instead of the mersalyl injection.

The theophylline caused a rapid fall in right auricular pressure and rise in cardiac output, beginning within 10 to 20 minutes and passing off in an hour. The mercurial diuretic caused a gradual fall in auricular pressure and, in all but 2 cases, a slow rise in output beginning about 2 hours after the injection and reaching a maximum in 5 to 7 hours. The highest level of output and lowest level of auricular pressure occurred either at or just after the period of maximum diuresis. Output then tended to return to the initial level faster than the auricular pressure rose. Pulse rate and blood pressure rarely changed significantly. Maximum diuresis occurred on the average 4½ hours after the injection was given.

Comparison with figures obtained by Howarth *et al.* (*Clin. Sci.*, 1946, **6**, 41) for venesection showed that the circulatory effects of mercurial diuretics in congestive heart failure are comparable with those obtained when the right auricular pressure is reduced mechanically (by venesection or application of constriction to thigh veins), but that the drugs act more slowly. It is therefore probable that the cardiac output rises because the auricular pressure falls. Whether a fall in circulating blood volume brings this about has yet to be proved. Reduction of oedema obviously cannot have played a part in the early stages of the circulatory effect. It is also possible that the drugs have a direct action on the cardiovascular system. *S. S. B. Gilder*

2582. **The Effect of Theophylline Ethylene Diamine on Renal Function in Control Subjects and in Patients with Congestive Heart Failure**

J. O. DAVIS and N. W. SHOCK. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 1459–1468, Nov., 1949. 1 fig., 31 refs.

The behaviour of the kidney in congestive heart failure is uncertain, and this report from Baltimore on sodium and water excretion after administration of a xanthine diuretic, theophylline ethylene diamine (TED), is an attempt to elucidate it. On 25 elderly control subjects who had neither hypertension nor renal disease and 6 patients with congestive failure an investigation was carried out while they were on a diet containing an undetermined quantity of sodium. Inulin and " diodrast " clearances were determined, with measurement of sodium excretion and venous pressure in some cases, both before and after intravenous injection of 0·48 g. TED either as a single dose or followed by slow infusion of 0·48 g. during the rest of the test. In controls uniform

results were obtained, with increase in filtration rate lasting up to one hour, variable slight increases in effective renal plasma flow and filtration fractions, and increases in urinary output and sodium clearance of up to three times. In the initial period sodium concentration was normal, but as urinary output fell it was approximately doubled. Of the patients with congestive failure four had a glomerular filtration rate within normal limits before the injection of TED and two a low rate, with reduction in urinary output and sodium clearance in five. After TED administration in those cases with a previously normal glomerular filtration rate the sodium excretion in urine was immediately increased, but in the other two it was essentially unchanged, although no constant change was noted in filtration rate or renal plasma flow such as occurred in the controls.

Venous pressure was reduced a little less in the patients than in the control group.

TED appears to increase sodium and water excretion by decreasing tubular absorption rather than by increasing glomerular filtration, and it is suggested that there is no evidence to show that oedema in congestive failure is due to low renal filtration. Rather there is tubular dysfunction with increased reabsorption of sodium and water, which may of course be brought about by extrarenal influences. *K. Gurling*

2583. **Influence of Heart-rate on Cardiac Output. Studies with Digoxin and Atropine**
H. G. KELLY and R. I. S. BAYLISS. *Lancet* [*Lancet*] **2**, 1071–1075, Dec. 10, 1949. 2 figs., 17 refs.

By measurement of the right auricular pressure and determination of the cardiac output the effect of intravenous administration of digoxin (0·75 to 1·5 mg. according to weight) in lowering the former and increasing the latter in patients with heart failure was confirmed in 27 patients. It is shown that these effects are the same whether the patient has a normal rhythm or auricular fibrillation and occur regardless of any slowing of the heart rate. The response of patients with no heart failure to intravenous injection of atropine (2 to 3 mg.) was by an increase in heart rate, and this was usually associated with a fall in right auricular pressure and an increase in cardiac output. A similar effect was noted in a few patients with heart failure. The administration of atropine an hour after digoxin to patients with heart failure had no adverse effect on cardiac output or venous pressure despite the fact that in the patients with auricular fibrillation it reversed the slowing effect of the digoxin. *C. Bruce Perry*

2584. **Long-term Results of the Treatment of Infective Endocarditis with Antibiotics.** (Les résultats éloignés de traitements antibiotiques des endocardites infectieuses)
M. B. MULLER. *Journal de Médecine de Lyon* [*J. Méd. Lyon*] **30**, 843–847, Nov. 5, 1949.

Eight cases of subacute streptococcal endocarditis and 2 cases of acute streptococcal endocarditis in patients with a previously healthy heart were treated with penicillin, with one death in the latter group. Three cases of subacute staphylococcal endocarditis were also treated, with two fatalities. Eight cases of subacute bacterial endocarditis with persistently negative blood cultures were treated, with 2 deaths. In none of the cases treated successfully was there a reappearance of septic phenomena during observation periods of between 1 year and 3 years. Penicillin sensitivity of the organism *in vitro* was not always a reliable guide to dosage, and clinical observation was considered to be more valuable. Rapid increase in dosage in resistant cases was felt to have prevented the emergence of resistant strains. One patient with acute streptococcal endocarditis in a previously healthy heart lost, after 2 years, all signs of valvular involvement. Persistent signs of renal involvement after eradication of the infection are considered a serious prognostic sign. *G. Schoenewald*

2585. **Isthmic Coarctation of the Aorta with Persistent Ductus Arteriosus.** (Rétrécissement isthmique de l'aorte avec persistance du canal artériel)
P. SOULIE, M. SERVELLE, J. HOREAU, and J. NOUAILLE. *Presse Médicale* [*Pr. méd.*] **58**, 137–138, Feb. 11, 1950. 5 figs.

A case of aortic coarctation associated with patent ductus arteriosus in a boy of 14 is described, in which the ductus opened into the aorta above the stricture (adult type), instead of below (infantile type) as in the majority of cases. In consequence, the blood flow was from the aorta into the pulmonary bed, with consequent congestion and dyspnoea on exertion. Angiocardiograms demonstrated this relationship pre-operatively, dye injected into the carotid artery appearing in the pulmonary circulation. Where a patent ductus opens below the stricture a mixture of venous and arterial blood is carried to the lower extremities, which may therefore be cyanosed—a finding absent in the present instance. Otherwise the signs were typical both of patent ductus (continuous murmur) and of coarctation (anastomotic vessels, rib-notching, and absent pulse and subnormal blood pressure in the legs).

At operation the left subclavian artery, which hid the aortic arch, was much dilated, as also was the aorta below the stricture. The ductus was wide but very short, pulling the aorta medially, and hence could not first be divided between ligatures. It was transfixed and tied on the pulmonary side, and then resected with the coarcted segment, followed by end-to-end anastomosis of the aorta. This rendered the 7-hour operation very difficult, but the end-result was good. *Geoffrey Flavell*

2586. **Congenital Communication Between Aorta and Pulmonary Artery. Report of a Case and Review of the Literature**
H. PERELMAN and W. G. J. PUTSCHAR. *Bulletin of the International Association of Medical Museums* [*Bull. int. Ass. med. Mus.*] **30**, 1–14, Nov., 1949. 2 figs., 42 refs.

2587. **Drainage of Pulmonary Veins into Coronary Sinus**
A. VASS and J. K. MACK. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **78**, 906–913, Dec., 1949. 5 figs., 7 refs.

2588. **Congenital Endocardial Sclerosis**
J. M. CRAIG. *Bulletin of the International Association of Medical Museums* [*Bull. int. Ass. med. Mus.*] **30**, 15–67, Nov., 1949. 25 figs., 26 refs.

CORONARY OCCLUSION AND ANGINA

2589. **Dynamics of Changes in the Coronary Circulation in Myocardial Infarction.** (Динамика изменений сосудов третьего круга кровообращения при инфарктах миокарда)
B. V. OGNEV. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 11, 37–45, Nov., 1949. 6 figs.

The coronary circulation is described in 50 human hearts, including 8 with myocardial infarction, and in the hearts of 86 dogs with experimental lesions, the results being presented in the form of a general discussion. The findings fall into two main groups, anatomical and pathological.

The anatomical findings were these. The coronary arteries vary both in extent and in distribution, which is inconstant even for secondary and tertiary branches. The main arterial anastomoses are of fifth-order branches; further branching leads to vessels of lesser diameter anastomosing by polygonal nets arranged according to the direction of the muscle bundles. Special branches to the auricles, pericardium, great-vein valves, and sino-auricular node are described; the branches to the ventricular walls are arranged according to the shape of the ventricles themselves. It is suggested that the subdivision of the heart wall be based on functional areas, as seen in infarction, rather than on purely anatomical findings. The vasa vasorum of the coronary vessels arise from the aorta and run in the direction of the vessels they supply, giving off straight and recurrent branches to the fifth order.

The pathological findings confirm the generally accepted ideas on the extent and local consequences of myocardial infarction. Stress is laid on myomalacia cordis and aneurysms in scars of infarcts.

[The photographs reproduced are rendered almost useless by poor contrast and coarse grain.]

Jeffrey Boss

2590. **Coronary Occlusion and Myocardial Infarction Associated with Chronic Rheumatic Heart Disease**
F. E. GARDNER and P. D. WHITE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **31**, 1003–1009, Dec., 1949. 9 refs.

At the Massachusetts General Hospital an analysis was made of findings at 6,000 consecutive necropsies. The analysis showed that 436 patients had died from rheumatic heart disease and that 513 patients had died from coronary disease. In 32 cases both conditions were present, but in only 7 of these cases was the correct diagnosis made before death. Moreover, in 21 of the patients suffering from the two conditions rheumatic carditis had escaped diagnosis during life. Among 10,000 cases of cardiovascular disease the clinical diagnosis of a rheumatic cardiac lesion with co-existent coronary disease was made in 57 cases. The presence of rheumatic disease was recognized in only 2% of patients with lesions of the coronary arteries, whereas the combined lesions were found in 6% of the series of necropsies on cases of coronary heart disease. On clinical examination the majority of combined lesions were discovered in elderly patients. It is not always easy to detect the presence of rheumatic heart disease in these patients, especially when there is no history of rheumatic fever. Even when auricular fibrillation is discovered the arrhythmia may not necessarily result from a rheumatic lesion. Usually little assistance is to be expected either from the radiological findings or from the electrocardiograms. Auscultation for the characteristic murmurs of mitral stenosis constitutes an important clinical aid. Sometimes the murmurs associated with a lesion of the aortic valve may be attributed to atherosclerosis instead of rheumatic disease.

It is considered that rheumatic heart disease plays no part in the pathogenesis of degeneration of the coronary arteries. This belief is supported by the fact that the series of necropsies did not include a single instance of the occurrence of combined lesions in a patient under 40 years of age. On the other hand, it must be borne in mind that the two conditions may co-exist.

A. Garland

2591. **Transfusion Treatment of Shock due to Myocardial Infarction**
F. H. EPSTEIN and A. S. RELMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **241**, 889–893, Dec. 8, 1949. 1 fig., 35 refs.

Clinical observations are reported on 50 patients in "shock" following coronary occlusion; 20 of these received a transfusion. The criteria of shock were a systolic blood pressure remaining below 90 mm. Hg for at least one hour associated with weakness or stupor, cyanosis, and coldness and dampness of the skin. For transfusion, an average of 700 ml. blood or plasma was usually given at the rate of 250 ml. per hour, starting 3 to 4 hours after the appearance of "shock". The authors conclude that, although transfusion seemed to be of benefit in a few cases, there was no significant difference between the two groups as regards mortality and recovery from shock. Transfusion did not seem to increase the incidence of pulmonary oedema or the severity of congestive failure. *R. T. Grant*

2592. **Cholesterol Content of the Coronary Arteries and Blood in Acute Coronary Artery Thrombosis**
L. M. MORRISON and K. D. JOHNSON. *American Heart Journal* [*Amer. Heart J.*] **39**, 31–34, Jan., 1950. 20 refs.

The authors suggest that a disturbance in lipid metabolism is a factor in the pathogenesis of atherosclerosis. This suggestion is based on the following findings: (1) The average cholesterol content of the coronary arteries in a group of patients who died from an acute coronary artery thrombosis was four times as great as the average cholesterol content of the coronary arteries in a comparable control group. (2) Hyper-

cholesterolaemia was found in most of the patients who died of coronary thrombosis, as compared with the average blood cholesterol level in the control group. *R. T. Grant*

2593. **Aspirin in the Treatment of Vascular Diseases**
P. C. GIBSON. *Lancet* [*Lancet*] **2**, 1172–1174, Dec. 24, 1949. 7 refs.

A questionary concerning the use of aspirin in the treatment of anginal pain was sent by the author to 22 doctors, of whom 20 replied. Rather more than 45 patients had been so treated by 15 of these, and the results are expressed in terms of the doctors' clinical impressions of the patients' subjective relief. No details were required of the type of case or method of prescription. Eight of the 15 doctors thought the treatment of undoubted value both in relieving and in preventing the pain, and none considered it useless. Reports are added of cases of chronic thrombophlebitis and of temporal arteritis which were successfully treated with the drug, and a scheme of dosage for cases of coronary thrombosis suggested [no case of this type is reported]. This consists of aspirin, gr. 20 (1·3 g.), and ascorbic acid, 50 mg., suspended in tragacanth, to be given 4-hourly after food (at night, after a drink of milk) for 10 days or until the erythrocyte sedimentation rate and leucocyte count are normal. At this stage the dose of aspirin is halved, that of ascorbic acid remaining unchanged, and this is the dosage recommended for other conditions. It is claimed that a prima facie case has been established for a more extensive trial of aspirin in coronary disease.

[Although these actual observations seem few and undetailed, the recognized effects of aspirin on pain threshold, prothrombin time, and erythrocyte sedimentation rate in other conditions probably justify its further trial in coronary disease.] *W. A. Bourne*

DISORDERS OF CIRCULATION

2594. **Treatment of Peripheral Vascular Disturbances by Administration of Histidine–Ascorbic-acid.** (Tratamiento de algunos trastornos circulatorios de los miembros por la administractión de histidina-ácido ascórbico)
A. RODRÍGUEZ ARIAS, A. S. PALAZZI, and F. VIDAL-BARRAQUER. *Angiologia* [*Angiologia, Barcelona*] **2**, 1–11, Jan.–Feb., 1950. 3 refs.

2595. **Observations on the Symptomatic Treatment of Chronic Vascular Headache with Cafergone (Ergotamine Tartrate and Caffeine)**
S. G. COHEN and L. H. CREIP. *New England Journal of Medicine* [*New Engl. J. Med.*] **241**, 896–900, Dec. 8, 1949. 12 refs.

2596. **The Pathogenesis of Vasomotor Headache and its Treatment with Dihydroergotamine (DHE).** (Zur Pathogenese und Therapie des vasomotorischen Kopfwehs mit Dihydroergotamin (DHE))
P. HOFMANN. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 28–31, Jan. 14, 1950. 26 refs.

2597. **The Action of Deoxycortone Acetate and Sodium Chloride in Rats with Experimental Hypertension.** (Die Wirkung von Desoxycorticosteronacetat und Kochsalz auf den experimentellen Hochdruck der Ratte)
F. GROSS. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **81**, 211–221, 1950. 2 figs., 10 refs.

Repeated injections of deoxycortone acetate (DOCA) increase the blood pressure of animals. In an attempt to obtain some evidence of the mechanism of this rise, the author observed the effects of DOCA and sodium chloride, together and separately, on the blood pressure of normal rats and that of rats with hypertension following temporary encapsulation of one kidney, the other kidney having been removed. Subcutaneous injection of 5 mg. DOCA per kg. in oil on alternate days for 3 months had no effect on the blood pressure of normal or hypertensive rats. Normal rats given additional sodium chloride in the diet and drinking water showed a mild increase in blood pressure compared with rats on a normal diet. In rats with experimental hypertension, sodium chloride alone caused no further rise in blood pressure. Both in normal rats and in those with hypertension DOCA and sodium chloride together caused an increase in the blood pressure during the 3 months. The effect was more prominent in the animals with hypertension.

The hypertensive effects of DOCA and sodium chloride and that of encapsulation are additive and are at least partly due to different mechanisms. This contention is supported by the difference in histological changes found in the kidneys. The changes due to DOCA and sodium chloride are mainly endarteritis and periarteritis, differing from the widespread degenerative changes in the kidney of rats after temporary encapsulation. *Derek R. Wood*

2598. **The Diet and Hypertension. A Review**
C. B. CHAPMAN and T. B. GIBBONS. *Medicine* [*Medicine, Baltimore*] **29**, 29–69, Feb., 1950. Bibliography.

2599. **Thiocyanate Therapy**
W. F. CONNELL, G. K. WHARTON, and C. E. ROBINSON. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **62**, 20–27, Jan., 1950. 4 figs., 14 refs.

In the past 20 years over 60 papers have been published on thiocyanate therapy of hypertension, and before 1936, when Barker reported the simple method of estimating sodium thiocyanate in serum, 9 cases of fatal poisoning were reported. It is suggested that the optimum dosage and the selection of suitable patients have not been adequately discussed in the literature. In the present study there were 140 subjects (50 out-patients from a hypertension clinic, 30 in-patients, 10 healthy interns, and 50 undergraduate medical students). If the normal size of the extracellular space is taken as 20% of the body weight and the thiocyanate radical is evenly distributed in this space, the following formula is reached: weight of patient (in lb.)×0·9 (constant)×desired serum level of thiocyanate in mg. per 100 ml.=mg. of potassium thiocyanate required to

" cyanate " the patient. Practical experiment suggested 1·7 in place of 0·9 as the constant in the formula. Furthermore, excretion studies suggest that indifferent absorption is a major factor governing the end result with oral administration. One of the authors found the following dose (on the basis of over 3 years' trial) satisfactory. A loading dose of twelve 200-mg. " enseals " of potassium thiocyanate was given, 4 enseals at 4-hour intervals. Serum thiocyanate level was estimated at the end of 24 hours from the first dose. For maintenance 1 enseal (200 mg.) was given twice or occasionally three times daily. Maintenance dosage is variable in different patients and in the same patient on different days. A 4- to 5-day observation period is thought to give adequate data for assessment of the value of this method in individual treatment. By this means levels in serum of between 8 and 14 mg. per 100 ml. can be obtained.

The drug is indicated in cases of severe headache, and is a " sovereign remedy " for this symptom. It is not primarily useful for reducing the blood pressure [other authors disagree]. Patients in group I of the Keith and Wagener classification are suitable for the treatment, and those in group II may, if the blood pressure falls, have some measure of protection from premature cardiovascular senescence.

The drug is contraindicated in groups III and IV and in malignant hypertension because renal failure may cause drug accumulation. It should not be given to patients over 60 years old because hypertension at this age is essentially benign and any therapy is meddlesome, or to patients with drug intolerance or cardiac and cerebral vascular complications. The drug is also contraindicated in all cases where adequate control of the serum level is impossible.

[The toxic effects noted are the same as those reported by other observers. This is a useful paper in that it throws light on a somewhat neglected method of therapy of hypertension which is safer than sympathectomy and almost certainly equally effective in selected cases.]

John Anderson

2600. **Studies in Arterial Hypertension.** (Estudos sôbre hipertensão arterial)

J. Ramos, S. Borges, S. Carvalhal, M. Iunes, and M. P. da Silva. *Arquivos Brasileiros de Cardiologia* [*Arch. brasil. Cardiol.*] **2**, 359–388, Dec., 1949. 15 figs., 46 refs.

In a short introduction the findings of various authors as regards changes in the renal and muscular arteries in essential hypertension are mentioned. The authors then discuss 25 cases of hypertension treated by sympathectomy, the patients being divided into 4 groups according to the degree of arterial damage. The authors do not attach any importance to the lumen-wall ratio but only to the qualitative changes. It was found that the changes in the renal arterioles were more advanced than those in the muscular (intercostal) arterioles. The patients' retinal arteries were examined with the Keith–Wagener classification in mind; the changes in these corresponded more to those in the muscular arteries than to those in the renal ones; thus in 10 cases fundal changes were less intense than renal ones. There was little relation between the levels of systolic and diastolic pressure and the responses to the Hines cold pressor test and barbiturate administration. The higher the blood pressure, the greater were the renal changes. The fall in blood pressure caused by barbiturates did not correspond to the severity of the renal lesion, but it was usually found that the greater the renal damage, the greater was the reaction to cold immersion. The various changes were then correlated with the state of the muscular arterioles. The authors regard the state of the muscular arterioles as being indicative of the general state of the general arterial tree and think that biopsy examination may be of some use in selecting cases for sympathectomy.

Tests of renal function—specific gravity and Van Slyke urea clearance test—did not yield results corresponding to the histology of the kidney; the authors plead, therefore, for more sensitive tests of renal function; they regard the relative rarity of death from uraemia in essential hypertension as being due to the great reserve of the kidney.

[A fair criticism of the paper is the small number of patients studied.] *Paul B. Woolley*

2601. **The Mechanism of the Vicious Circle in Chronic Hypertension**

F. B. Byrom and L. F. Dodson. *Clinical Science* [*Clin. Sci.*] **8**, 1–10, 1949. 3 figs., 16 refs.

There is some evidence that in experimental renal hypertension the mechanism by which the pressure is maintained changes with the passage of time. If now the Goldblatt experiment be modified by removal of one kidney and subsequent clamping of the opposite renal artery, and if, after an adequate period, the clamp be removed, then disappearance of the hypertension would indicate that no independent extrarenal mechanism was maintaining the blood pressure at a high level. Persistence of the hypertension would, of course, not necessarily prove the converse, because permanent ischaemic damage to the kidney might have occurred.

This theory was tested on young albino rats in which after right nephrectomy a silver clip was placed on the left renal artery so as partly to occlude the vessel. After 4½ to 32 weeks the clip was removed. Blood pressure was measured at intervals, and 4 weeks after removal of the clip each animal was killed and the organs studied histologically.

Of 84 rats 63 developed sustained hypertension after application of the clip. The incidence of complications (cardiac and cerebral crises) was higher than in the Goldblatt experiment, and 27 rats died before the clamp could be removed. In 23 of these the kidney was examined and appeared normal macroscopically and, in 16 cases, microscopically as well. In the other 7, lesions were trivial. This contrasts with the atrophy of the ischaemic kidney when the second one is intact. Apparently when the whole renal territory is threatened with ischaemia the effort to compensate for this is relatively greater.

After the clamp had been removed, in all but one rat the blood pressure fell to normal within 24 hours and remained normal. This contrasts with the frequent

persistence of hypertension in a rat with a second kidney. When the clip was removed during a vascular crisis relief of symptoms occurred in a few hours.

At necropsy in rats killed at least 4 weeks after removal of the clip there was no evidence of progressive vascular necrosis and the kidney was either normal or almost so. The cardiac hypertrophy present during the hypertensive phase had receded.

It is inferred that no extrarenal mechanism intrudes in chronic renal hypertension, and that hypertension is irreversible only if there is extensive irreparable damage to both kidneys. Hypertension in man may be divided into: (1) renal hypertension due to bilateral primary renal disease and incurable; (2) hypertension due to unilateral renal disease, in which removal of the affected kidney should cure the condition if the other is not already secondarily damaged; (3) malignant essential hypertension, which correction of an unknown primary abnormality might be expected to cure; (4) benign essential hypertension, in which as yet no light has been thrown on the ability of the damaged kidney to perpetuate hypertension. *S. S. B. Gilder*

2602. **The Effect of a War-imposed Protein Free Diet on the Blood Pressure Level in Essential Hypertension**
J. KOHÁRI-KUCHÁRIK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **219**, 27–29, Jan., 1950. 6 refs.

Almost complete protein-starvation during the 10 months following the siege of Budapest in 1945 was found to have had no effect on the blood pressure of 39 patients with essential hypertension observed by the author throughout this period. *G. Schoenewald*

2603. **Leucotomy and Hypertension. A Case Report**
R. W. TIBBETTS. *British Medical Journal* [*Brit. med. J.*] **2**, 1452–1454, Dec. 24, 1949. 10 refs.

The case is reported of a woman aged 54 suffering from severe depression with suicidal tendencies. Also present was a well-marked but still labile hypertension, blood pressure varying on different occasions from 170/100 to 260/160 mm. Hg. On psychiatric grounds bilateral leucotomy was performed, and although very severe arterial haemorrhage occurred on the left side during operation post-operative progress was uneventful; the patient was no longer depressed and was able to return to her household duties. Blood pressure had fallen 16 months after operation to within the range 160/100 to 140/95 mm. Hg, and although arteriosclerotic disk changes remained, no retinal exudates or haemorrhages were present (a small retinal haemorrhage had been observed pre-operatively).

It is suggested that this fall in blood pressure might be due to: (1) Prolonged rest in bed; as the patient had been at rest for a prolonged period before operation this reason did not apply here. (2) Operative interference with anatomical areas concerned with automatic function; too little is known of this to draw conclusions, especially in view of the extensive haemorrhage which occurred in this case. (3) Relief of mental tension; this is considered to be probably an important factor.

A few suggestions are put forward as regards the indications for performing prefrontal leucotomy when hypertension is also present. *J. B. Wilson*

2604. **The Effect of the Rice Diet on the Level of the Blood Pressure in Essential Hypertension**
D. G. LOOFBOUROW, A. L. GALBRAITH, and R. S. PALMER. *New England Journal of Medicine* [*New Engl. J. Med.*] **240**, 910–914, June 9, 1949. 22 refs.

The authors here present an interim report on the treatment of essential hypertension in out-patients with rice diet. By frequent estimation of the 24-hour urinary chloride excretion, the patients' adherence to the diet was checked, "strict adherence" being marked by an excretion of 10 mEq. or less per litre. Out of 56 patients 16 were thus classified as "strict adherents". The periods of treatment varied from 3 to 54 weeks. In the strict adherents a loss of weight and fall in blood pressure resulted.

[The chief value of this paper lies in its demonstration that adherence to a palatable salt-free diet can be maintained in a moderate number of out-patients. The actual results themselves appear to be comparable with the initial results of any new treatment.] *W. T. Cooke*

See also Section Pharmacology and Therapeutics, Abstract 2404.

BLOOD VESSELS

2605. **Arteriosclerosis Obliterans as a Cause of Ulcers of the Leg**
S. I. SHAPIRO and R. NOMLAND. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **61**, 80–88, Jan., 1950. 4 figs., 11 refs.

Chronic ulcers of the leg are a constant problem in the aged. At the University Hospitals of the State University of Iowa over a period of 3 years the authors investigated 52 cases, in 10 of which the chief cause of the ulceration was diminished arterial circulation due to obliterating arteriosclerosis. In this series the diagnosis was based on history and objective findings. The simplest and most reliable sign of partial or complete closure of the arteries of a limb is inability to palpate the pulse. Oscillometric readings were found to be much lower than normal in all cases of arterial occlusion. Other diagnostic criteria used were the appearance of the skin and nails and the presence of osteoporosis as seen radiologically. A subjective sensation thought to be diagnostic was pain on exercise, mainly of the intermittent-claudication type. Pain was found to be more common in ulcers due to arteriosclerosis than in ulcers due to venous stasis.

Of the 10 patients with arteriosclerotic ulcers 7 were men. The average age of the whole group was 65·7 years, which is in the age group in which the highest incidence of arteriosclerosis occurs. The duration of the ulcers varied widely, the average being 2 years. Cultures taken from the surface of the ulcers shed no light on their aetiology, and neither position nor appearance was specific. No history or evidence of thrombophlebitis,

varicosities, oedema, or siderosis indicating chronic venous insufficiency was found. Two of the ulcers were definitely painful, others were tender in varying degree. In the discussion of differential diagnosis stress is laid on the importance of negative findings. Treatment by skin grafting (pinch type) was successful in 9 of the 10 cases described. *H. S. Laird*

2606. **Peripheral Arterial Embolism. Treatment with Heparin–Papaverine.** (Perifere arterie-embolier. Med særligt henblik pa behandlingen med heparin-papaverin) B. SOMMER PEDERSEN. *Nordisk Medicin* [*Nord. Med.*] **42**, 1957–1960, Dec. 23, 1949. 9 refs.

Eight cases of peripheral arterial embolism were treated with heparin and papaverine, the latter being given intravenously in doses of 30 mg. 4- to 6-hourly for 2 days and then 3 times daily for one week. One patient with an embolus in the femoral artery and another with multiple emboli died. In the remaining 6 cases the treatment was completely successful. The author suggests that this treatment is indicated in all cases of arterial embolism in the leg and forearm, in all cases of embolism in which the patient's condition does not permit operation, and in all cases admitted more than 24 hours after the event. Embolectomy is indicated when the aorta or the iliac or femoral arteries are involved, and in other cases when medical treatment does not rapidly improve the circulation. Anticoagulant therapy should be employed before and after operation. *B. Nordin*

2607. **Anticoagulant Therapy with Depot Heparin.** (Traitement anticoagulant par l'héparine " retard ") P. PUNDEL. *Presse Médicale* [*Pr. méd.*] **57**, 1120–1121, Dec. 3, 1949. 1 fig., 17 refs.

The author, working in the Gynaecological Clinic of the University of Brussels, reviews the various methods used to prolong the effects of heparin and describes his own experience with a combination of heparin (25 parts) and polyvinylpyrrolidone (75 parts), to which is added procaine (4 parts), to make the injection painless and to augment the retarding effect of the polyvinylpyrrolidone. The injection, in 5 ml. of distilled water, is given subcutaneously at a depth of 3 to 4 cm. into the outer thigh. For prophylaxis in obese females aged 40 and over with varicose veins or cardiovascular insufficiency, or in females with a previous history of thrombophlebitis, a dose containing 200 mg. of heparin is given. The clotting time is previously estimated by Lee and White's method, and is repeated 3 hours after the injection, when it is usually 40 to 60 minutes. It is again estimated at 24 and 48 hours and further injections are given if the clotting time falls below 20 minutes. For treatment, 200 mg. of heparin as " depot heparin " is given at the earliest suspicion of thrombosis, 50 mg. of ordinary heparin being given intravenously if embolism has already occurred. If the clotting time has not reached the required level 3 hours later, a further 100 mg. of depot heparin is given. One injection every 48 hours is usually adequate, treatment being continued for 3 weeks. Large doses are contraindicated where there is renal insufficiency or a haemorrhagic tendency, but heparin is not contraindicated during menstruation or the puerperium. Depot heparin is neutralized by digitalis, but not by strophanthin. The antidote recommended in the case of overdosage is 40 mg. of 1% protamine sulphate, given intravenously and repeated if necessary. The advantages claimed for this preparation are less frequent injections and less expense, as only a quarter of the usual dosage of heparin is required.

[This appears to be an advance in anticoagulant therapy, but the number of patients treated is not stated.] *I. Ansell*

2608. **Use of Hyaluronidase in Preventing the Pain of Subcutaneous Heparin Injection**
M. S. TUCHMAN and S. E. MOOLTEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **219**, 147–151, Feb., 1950. 1 fig., 14 refs.

When heparin is injected subcutaneously it may cause ecchymosis and persistent pain at the site of injection. However, the authors claim that pain can be either eliminated or reduced to a minimum by the preliminary infiltration of the site with a solution of hyaluronidase. The adoption of this technique makes it possible for the injection of heparin to be given by the nursing staff, the effect on coagulation time of heparin given subcutaneously not differing substantially from that found when the drug is given by intermittent intravenous injection.

In a series of experiments an area of subcutaneous tissue was infiltrated with 10 ml. of a sterile solution of hyaluronidase prepared by dissolving 1 mg. of the dried enzyme in 100 ml. of normal saline. Then heparin solution (10 mg. per ml.) was injected at the same site every 4 hours in doses which ranged from 25 to 50 mg. Pain was not produced by the injections until more than 12 hours had elapsed since the hyaluronidase infiltration. In subsequent experiments the subcutaneous tissue was infiltrated gradually with 5 ml. of the hyaluronidase solution before each heparin injection, which was given through the same needle, a fresh site being used on each occasion. There was practically no discomfort provided the heparin solution was injected slowly. Whereas persistent pain ensued when 10 to 20 mg.of heparin was injected without the preliminary administration of hyaluronidase, after the preliminary injection of hyaluronidase as much as 100 mg. of heparin could be injected painlessly. At first the hyaluronidase solution was freshly prepared each day; later on it was found that the solution, if kept in the refrigerator, remained effective even after 3 days.

An interesting incidental observation was made in the case of an elderly woman suffering from coronary thrombosis. Intravenous injections of heparin had caused venous thrombosis and a large, painful haematoma at the site. Not only was the pain relieved by infiltration of the area with hyaluronidase, but the haematoma was almost entirely absorbed within 3 hours. *A. Garland*

2609. **Phlebitis and the Diagnosis of Thromboangiitis Obliterans**
E. A. EDWARDS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **31**, 1019–1023, Dec., 1949. 1 fig., 5 refs.

Disorders of the Blood

2610. **Blood and Bone Marrow Studies in Renal Disease**
I. R. CALLEN and L. R. LIMARZI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 3–23, Jan., 1950. 4 figs., bibliography.

This paper describes an investigation of the blood and bone marrow of 102 patients with nephritis or other renal disease, or essential hypertension. In 44 patients with nitrogen retention due to renal disease, the degree of anaemia present was related to the degree of nitrogen retention. The anaemia was usually normocytic and normochromic. The bone marrow was hypercellular in 80% of patients with renal disease and azotaemia. Hypoplasia of the erythroid tissue was observed only when the concentration of non-protein nitrogen in the blood was above 150 mg. per 100 ml. It was never marked, and there was no depression of leucocyte or platelet production. It is therefore concluded that the finding of a cellular bone marrow in cases of chronic glomerulonephritis is of no prognostic significance.

A. Brown

2611. **Disturbances of Blood Coagulation Caused by Endogenous Anticoagulants in Hyperglobulinaemia.** (Blutgerinnungsstörungen durch körpereigene Antikoagulantien bei Hyperglobulinämie)
E. LÜSCHER, A. LABHART, and E. UEHLINGER. *Helvetica Medica Acta* [*Helv. med. Acta*] **16**, 283–286, Sept., 1949. 1 fig., 3 refs.

Hyperproteinaemia and abnormal coagulation of the blood were observed in 2 cases, in one of which diffuse plasmocytoma had been diagnosed with certainty, while in the other the diagnosis was of either plasmocytoma or chronic interstitial myelitis. Dilution of the blood rendered the coagulation normal. When blood from one of these patients was added to blood from a normal subject the latter sample also coagulated abnormally. The clots were oily or gelatinous. Thrombin was normally formed and calcium, thrombocytes, and fibrinogen were present in normal amounts. There was evidently a factor present which interfered with coagulation. This was identified as a protein present in the β and γ fractions of the plasma proteins. Such disturbances of coagulation are not the general rule in the (frequently-occurring) hyperproteinaemia of plasmocytoma. *C. L. De Jongh* (*Excerpta Medica*)

2612. **Replacement Transfusions in the Treatment of Acute Leukaemia**
H. H. HENSTELL, I. S. HENSTELL, P. F. SALISBURY, and J. H. MILLER. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **3**, 371–379, Nov., 1949. 1 fig., 9 refs.

Three cases of acute lymphocytic leukaemia and one of aleukaemic lymphocytic leukaemia were treated by replacement transfusion as suggested by Bessis and Bernard (*Bull. Soc. méd. Hop. Paris*, 1947, **28**, 871). In one case there was a severe fatal reaction, but in the other 3 cases improvement followed the replacement transfusions, although the exact part they played is uncertain because folic-acid antagonists had been given before. The results suggest that normal blood contains anti-leukaemic factors which appear to be present in greater amounts in polycythaemia.

Two hypotheses of the mode of action are put forward: (*a*) that the leukaemia cells are stimulated to mature in a normal way, or (*b*) that the normal blood supplies substances in the absence of which abnormal cell proliferation occurs. If the second and more probable hypothesis be true, leukaemia must be a deficiency disease. *A. Piney*

2613. **Aminopterin (4-Aminopteroylglutamic Acid) Therapy in Leukemias**
O. B. HUNTER and G. J. CARROLL. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **3**, 380–384, Nov., 1949. 2 figs., 3 refs.

A report is given of 17 cases of acute leukaemia treated with aminopterin with results similar to those previously published. It is suggested that the total initial dose of aminopterin must be sufficient to neutralize the folic acid in the body, and that maintenance dosage must be sufficient to suppress the proliferation of excessively active cells but insufficient to inhibit the proliferation of cells dividing at a normal rate. It is for this reason that aminopterin is of little or no use in the chronic leukaemias; in them, the leukaemic cells are not proliferating much more rapidly than are the normal ones and the differential effect of aminopterin cannot therefore manifest itself.

The importance of dealing with intercurrent infection is stressed, and theories to account for the gradual failure of aminopterin therapy are propounded.

A. Piney

2614. **Mediterranean (Cooley's) Anæmia in Australia**
A. H. TEBBUTT. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 50–52, Jan. 14, 1950. 5 refs.

Two cases seen in Sydney are described in which a diagnosis of Cooley's (Mediterranean) anaemia is put forward. The first patient was a woman " aged thirty to forty years " of Lebanese origin who had suffered from an anaemia for at least 4 years. Examination of her blood proved the presence of a hypochromic microcytic anaemia with the existence of microcytes, poikilocytes, target cells, oval cells, and macrocytes with central pallor. There was increased resistance to hypotonic saline. The father of the patient had a hypochromic and microcytic anaemia and a target-cell and oval-cell trait. No examination of the patient's or the father's bone marrow was carried out, nor was any other member of the patient's family investigated.

The second case was that of a man aged 54, born in Greece. He had had splenomegaly and hepatomegaly and a blood dyscrasia for 3 years. Examination of his blood proved the presence of a microcytic hypochromic anaemia, with a leucocytosis (28,000 per c.mm., of which 76% were segmented and 6% band forms) and oval cells and target cells and poikilocytes. Large cells with pale centres, large normochromic cells, and fully haemoglobinized microcytes suggestive of spherocytes were also seen. Platelets were very numerous and formed clumps. In this case also there was an increased resistance to hypotonic saline. Biopsy examination of sternal marrow revealed the presence of a cellular marrow with increase in megakaryocytes; amongst the more immature myeloid series were numerous leucocytes. No member of this patient's family was examined. The author, realizing the unusual features of this case, suggests that there may have been another type of bone marrow dyscrasia with splenomegaly, hepatomegaly, and megakaryocytosis—possibly a myeloid metaplasia—arising coincidently in one of the Greek race with the background of the familial target-cell and oval-cell trait.

I. H. Milner

2615. **Treatment of Malignant Lymphogranuloma and Related Conditions with Nitrogen Mustard.** (Behandeling van lymphogranuloma malignum en verwante toestanden met methyl-bis-chloroaethylamine ("Nitrogen Mustard"))
J. GROEN, E. G. GODFRIED, G. K. L. KROMSIGT, J. H. REISEL, and S. TILLEMA. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 2681–2682, Aug. 6, 1949. 15 refs.

Of 15 patients treated with nitrogen mustard, 7 with Hodgkin's disease and one with lymphosarcoma showed distinct improvement, and one patient with reticulosis showed slight improvement. The indications for this treatment are listed provisionally as follows: generalized foci; high temperature not to be accounted for by the findings on examination; residual manifestations after the highest permissible dose of radiation; and cases resistant to irradiation. *S. J. de Vries* (*Excerpta Medica*)

2616. **Calciferol Treatment of Boeck's Sarcoid.** (Foreløbige erfaringer med ultranolbehandling af Boecks sarkoid)
I. GILG. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **111**, 1281–1285, Nov. 17, 1949. 2 figs., 22 refs.

Preliminary impressions are given of the results of vitamin-D_2 therapy for Boeck's sarcoid, as carried out at the Finsen Institute, Copenhagen. Most of the 42 patients so far treated showed considerable improvement, but toxic reactions were not uncommon and in some instances were severe. In addition to emphasizing the need for constant careful supervision during treatment, the author recommends the giving of lower doses than have been used elsewhere (90,000 i.u. at the outset, subsequent dosage to be modified according to progress and reactions). Treatment of Boeck's sarcoid with vitamin D_2 seems more promising than any of the methods previously employed. *W. G. Harding*

ANAEMIA

2617. **Intravenous Iron Therapy.** (Intraveneuze ijzertherapie)
J. GERBRANDY. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 4020–4028, Nov. 26, 1949. 2 figs., 7 refs.

Nine patients with hypochromic anaemia received 5 to 10 ml. of ferric saccharate (=100 to 200 mg. iron) daily intravenously. The haemoglobin value immediately began to rise (by 1 to 4% per day), a reticulocyte crisis (6 to 26%) occurred, and the erythrocyte volume rapidly became normal. In hypochromic anaemia the volume of circulating blood is often low. In 3 cases this volume was determined before and after iron treatment; in 2 an increase had occurred, showing that the production of haemoglobin was greater than appeared from its direct determination. One patient proved to have used 1·2 g. of the administered 2 g. for haemoglobin production; the other had used 1 g. of the 1·2 g. administered.

When the solution was injected rapidly, patients complained of backache, probably due to haemolysis, and vasodilatation (with reddening of the skin and a feeling of heat) was accompanied by a transient rise in blood pressure. This iron preparation also tends to cause venous thrombosis, for which reason it must be injected very slowly and into a different vein each time. The initial dose used was 50 mg. of iron and not more than 200 mg. per injection was given, to a total of 2 g. The preparation of this solution of ferric saccharate is described by de Vaal and Diepenhorst (ibid., 1949, **93**, 4029). *J. C. J. Burkens* (*Excerpta Medica*)

2618. **The Anti-anaemic Action of Cobalt.** (A cobalt antianaemiás szerepe)
L. DABIS, I. VITÉZ, and K. SZÉREMI. *Orvosi Hetilap* [*Orv. Hetil.*] **90**, 534–536, Sept. 4, 1949. 13 refs.

In view of the action of cobalt-containing vitamin B_{12} in pernicious anaemia, experiments were carried out to see whether cobalt alone had an anti-anaemic action. Inorganic cobalt salts being too toxic, the authors used cobalt citrate 1% and 0·1% in buffered solution, either injected subcutaneously or given orally to healthy white rats. No toxic effects were noted. The treated rats showed a rise in erythrocyte count to 80% above that of controls. *Dushanka Wolstenholme*

2619. **Roentgen Findings in Sickle-Cell Anemia**
D. S. CARROLL and J. W. EVANS. *Radiology* [*Radiology*] **53**, 834–844, Dec., 1949. 18 figs., 50 refs.

The tendency of the bone marrow to produce sickle cells is an inherited Mendelian dominant character almost confined to the negro race, in which its incidence is 7·5%. About 1 in 40 of those affected produce enough abnormal forms to give rise to the clinical picture of sickle-cell anaemia, the elongated erythrocytes being treated as foreign bodies and destroyed. The essential histological lesion is a capillary block, presumably due to failure of the abnormal erythrocytes to negotiate the narrower blood channels, this giving rise to engorgement and thrombosis followed by necrosis and fibrous replace-

ment. The symptomatology is very diverse, varying according to the organs affected, but pain in the bones and joints, fever, and the effects of cardiac impairment are commonly found, the condition tending to mimic rheumatic fever. Headache and other neurological signs may also be present.

Radiological changes were found in the skeleton in rather more than one-half of a series of 49 cases examined by the authors. The long bones showed changes in architecture; in some cases thinning and in other cases thickening of the cortex was seen. Increase in calcification and periosteal reaction were found in a few cases. Trabeculation was coarse and irregular, and osteoporosis, with softening of the vertebral end plates and their depression by the intervertebral disks, was a characteristic finding in the spine. Osteoporosis of the skull and a thickened calvarium were found in some cases, this tending to be localized and symmetrical. Vertical striations of the skull were uncommon, but striking when seen. Pathological findings in the chest included cardiac enlargement and, in the lung fields, evidence of oedema or congestion, or the patchy mottling of thrombosis.

The authors conclude that the *x*-ray findings may occasionally be sufficiently marked to be diagnostic in a hitherto unsuspected case of sickle-cell anaemia but that more frequently they are not more than suggestive.

A. M. Rackow

PERNICIOUS ANAEMIA

2620. **Nutritional Megaloblastic Anaemia: So-called Pernicious Anaemia of Pregnancy: a Preliminary Report**
B. V. KOTHARI and Y. M. BHENDE. *Indian Journal of Medical Research* [*Ind. J. med. Res.*] **38**, 347–363, July, 1949. Bibliography.

A detailed analysis of 40 cases of so-called pernicious anaemia of pregnancy was made in Bombay: spherocytosis and increased fragility were not constant and the only reliable diagnostic criterion is the finding of true megaloblasts in peripheral blood and marrow. This is true also of the pernicious anaemia of pregnancy seen in temperate climates, which on all grounds is similar to that seen in the tropics. As it can occur in non-pregnant females and males of any age it should be called nutritional megaloblastic anaemia. *G. M. Findlay*

2621. **Variable Response to Vitamin B_{12} of Megaloblastic Anemia of Infancy**
C. W. WOODRUFF, H. W. RIPY, J. C. PETERSON, and W. J. DARBY. *Pediatrics* [*Pediatrics*] **4**, 723–729, Dec., 1949. 3 figs., 8 refs.

The cases are reported of 3 children aged 17, 9, and 12 months, who had severe megaloblastic anaemia associated with manifestations of defective nutrition. Vitamin B_{12} was given parenterally in doses of 25, 25, and 30 μg. respectively. Haematopoietic response was satisfactory in the first 2 cases, but in the last case there was no significant response and the sternal bone marrow remained megaloblastic. This patient was then given intramuscular injections of folic acid, 5 mg. daily, to which she responded satisfactorily. It is suggested that "megaloblastic anaemia of infancy may not be a single entity, but rather a syndrome, some cases of which respond to one of the newer haemopoietic vitamins while other cases respond to another". [A number of instances have now been reported of megaloblastic anaemias, not of the classical Addisonian type, responding to folic acid after failing to do so to vitamin B_{12}.]

L. J. Davis

2622. **Vitamin B_{12} in Pernicious Anaemia: Parenteral Administration**
C. C. UNGLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1370–1377, Dec. 17, 1949. 8 figs., 23 refs.

Seventy-three responses to single doses of vitamin B_{12} injected intramuscularly were observed in 53 patients with pernicious anaemia in relapse. Doses were graded logarithmically from 1·25 to 160 μg. Conclusions are based on the means of a number of responses at each dose level. Reticulocyte responses were compared with the "expected" response to liver extract according to Isaacs and Friedman, but a better yardstick was the increase of red blood cells in 15 days.

While doses of 1·25 μg. had little or no effect, 2·5 μg. produced a definite but small response. Responses to 5 and 7 μg. were on average somewhat below, and to 10 μg. just up to expectation, both in respect to reticulocytes and to increase of red blood cells in 15 days (Della Vida and Dyke, formula for "average" group). Only in this limited sense can 10 μg. be regarded as a minimal effective dose. Larger doses produced still greater increase of red blood cells in 15 days, the mean response being roughly proportional to the logarithm of the dose, at least in the range 5 to 80, or possibly even 160 μg. From a formula devised to express this relationship the expected response to any dose within the range was calculated. Most of the responses actually obtained did not differ from the expected response by more than 330,000 per c.mm. Further tests at high and low levels of dosage are needed to complete the dose response curve, which will probably be sigmoid in form, rising gradually, then steeply, from the threshold dose, and flattening out to a horizontal level when supramaximal doses are reached.

Maintenance doses of 10 μg. of vitamin B_{12} every 2 weeks were satisfactory in 18 out of 21 patients followed for 6 to 15 months. The exceptions were 3 patients whose sore tongue was not completely relieved, one having macrocytosis in addition. Six women developed iron deficiency at 8 to 15 weeks, relieved by ferrous sulphate. Fresh neurological symptoms did not develop. Direct evidence of an effect in subacute combined degeneration is to be published elsewhere.—[Author's summary.]

2623. **Effect of Vitamin B_{12} on the Urinary Phenol Fractions in Pernicious Anemia**
L. D. ABBOTT and G. W. JAMES. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **35**, 35–42, Jan., 1950. 4 figs., 13 refs.

This work follows up that of Swendseid *et al.* (*J. Lab. clin. Med.*, 1947, **32**, 1242), who found that the treatment

of pernicious anemia with either liver or stomach preparations lowered the excretion of hydroxyphenol derivatives in the urine. The authors divide the ether-soluble urinary phenols into a bicarbonate-soluble fraction A, comprising the hydroxyphenols, and fraction B, insoluble in bicarbonate but soluble in sodium hydroxide, which represents the other phenols. The A : B ratio was raised in three out of four patients with pernicious anaemia.

On treatment of the patient with vitamin B_{12} (20 or 10 μg. on the first day followed by 5 μg. every day, and after one week every second day) the ratio fell—in one case after and in 2 cases before the onset of the reticulocyte response. The fourth patient, in whom the A : B ratio was not raised at the beginning, reacted to vitamin B_{12} with an increase in A : B ratio rather than with a fall. *H. Lehmann*

2624. **Refractory Pernicious Anaemia. Report of a Case Resistant to Vitamin B_{12}.** (Refractaire pernicieuze anaemie. Mededeling van een geval, refractair tegen vitamine B_{12})
C. K. V. VAN DOMMELEN. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 4043–4046. Nov. 26, 1949. 1 fig., 7 refs.

A case of pernicious anaemia (hyperchromic anaemia, with 44% haemoglobin, achylia gastrica, glossitis, numerous megaloblasts in the bone marrow, no increase of fat excretion, and no tract degeneration of the spinal cord) in an 83-year-old woman was treated with three 10-μg. doses of vitamin B_{12} and later with 8 doses of 4 ml. "pernaemon forte". Neither of these substances had any effect; no reticulocyte crisis occurred, the serum iron level showed no fall, and the haemoglobin and the erythrocyte count remained unchanged, as did also the clinical condition. When 10 mg. per day of folic acid was given a reticulocyte crisis promptly appeared, all the other abnormalities regressed, and the patient recovered. The vitamin-C content of the blood was 0·54 mg. per 100 ml.; this was not appreciably changed by administration of vitamin C with the folic acid.
J. C. J. Burkens (*Excerpta Medica*)

2625. **Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia. XI. Hematopoietic Activity in Pernicious Anemia of a Beef Muscle Extract Containing Food (Extrinsic) Factor upon Intravenous Injection without Contact with Gastric (Intrinsic) Factor**
F. H. GARDNER, J. W. HARRIS, R. F. SCHILLING, and W. B. CASTLE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 1502–1511, Nov., 1949. 1 fig., 23 refs.

The earlier classic researches of Castle and his colleagues on the extrinsic and intrinsic anti-anaemic factors, and their more recent observations that the haematopoietic activity of refined liver extracts and of vitamin B_{12}, when given by mouth, is enhanced by the simultaneous administration of normal human gastric juice prompted the authors to seek answers to the following questions: (1) Can extrinsic factor alone (as present in beef muscle) act directly as the antipernicious-anaemia principle when injected parenterally in a suitable form? (2) Is the potentiating action of intrinsic factor (gastric juice) specific only for vitamin B_{12} and chemically similar substances, or does it also influence the haematopoietic effect of other substances?

A concentrated extract of beef muscle (10 ml. derived from 400 g. of muscle) was prepared by extraction with water and alcohol [details are given in the paper], and was given to 7 patients with pernicious anaemia. It was given in daily doses of 10 ml. over 10-day periods, and the haematopoietic effect observed by means of serial reticulocyte counts. When the extract was given orally, diluted with saline, a detectable reticulocyte response occurred in only one instance. When it was given orally together with 150 ml. of normal human gastric juice, a reticulocyte response occurred in each of the 4 patients receiving it. The extract was subsequently given intravenously without gastric juice to 3 of these patients and induced a second reticulocyte response in each case, thus indicating greater haematopoietic activity on intravenous than on oral administration of the extract alone. Further observations on 2 patients showed that the haematopoietic effect of daily intravenous injection of 10 ml. of the beef muscle extract was less than that of similar injections of 1 μg. of crystalline vitamin B_{12}, and microbiological assays indicated that 10 ml. of beef extract contained from 0·37 to 0·9 μg. of vitamin-B_{12} activity.

The potentiating effect of normal human gastric juice on the beef extract given orally was surprisingly great compared with its effect on 5 μg. of vitamin B_{12} observed in previous experiments. This suggests that haematopoietic substances in meat extract other than vitamin B_{12} may be susceptible of potentiation by normal human gastric juice. On the other hand, experiments with glucose, L-tyrosine, and casein produced no evidence that their intestinal absorption was promoted by gastric juice, nor was there any evidence that gastric juice increased the haematopoietic action of pteroylglutamic acid when given orally. *L. J. Davis*

2626. **A Preliminary Study of the Relationship Between *Lactobacillus lactis* Dorner Response and Clinical Antipernicious Anemia Activity of Liver Extracts**
W. F. WHITE, J. R. MOTE, and E. E. HAYS. *Blood* [*Blood*] **4**, 1357–1360, Dec., 1949. 5 refs.

HAEMOLYTIC ANAEMIA

2627. **Haemolytic Anaemia with Panmyelopathy and its Pathogenesis.** (Hämolytische Anämien bei Panmyelopathie und ihre Pathogenese)
O. ROTH and B. JASIŃSKI. *Helvetica Medica Acta* [*Helv. med. Acta*] **16**, 531–547, Dec., 1949. 5 figs., 11 refs.

The authors give a detailed report and discussion of 3 cases of acquired haemolytic anaemia in which the marrow was hypoplastic and the spleen overactive. In 2 cases splenectomy was followed by almost complete cure while in one case the operation produced a complete remission for 6 weeks. The condition of the marrow is

attributed to splenopathic inhibition while it is supposed that the haemolysis was due to hypersplenism. [There is no reference to the presence of agglutinins or haemolysins in the serum, and the exact status of the cases is uncertain.] *A. Piney*

2628. **Haemolytic Macrocytic Anaemia due to Incomplete Antibodies.** (Over haemolytische macrocytaire anaemie door onvolledige antilichamen)
J. VANDENBROUCKE. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 3374, Sept. 24, 1949.

The Coombs test is used for the detection of incomplete antibodies. The case here reported was one of five of acquired haemolytic jaundice in which the result of the Coombs test was positive, while in 15 cases of congenital haemolytic jaundice it was negative. These unusual antibodies, however, are not found in all cases of acquired haemolytic jaundice. The cold-agglutinins also react differently to the Coombs test. The incomplete or unusual antibodies detected by means of the Coombs test cause damage to the erythrocytes because the osmotic resistance is lowered. The serum of the patient under discussion (group O) gave a positive reaction to the Coombs test with 21 test-samples of erythrocytes, also from group-O blood. From this it was concluded that the blood of these 21 donors, although belonging to group O, was unsuitable for transfusion to the patient in question. This finding accounts for the fact that in acquired haemolytic jaundice or anaemia the effect of transfusion is frequently unsatisfactory or positively unfavourable. The only chance of success in such cases is with transfusion of blood that has also passed the Coombs test for suitability.

J. J. de Jong (*Excerpta Medica*)

2629. **Diagnosis and Mechanism of Hemolysis in Chronic Hemolytic Anemia with Nocturnal Hemoglobinuria**
J. V. DACIE. *Blood* [*Blood*] **4**, 1183–1195, Nov., 1949. 2 figs., 18 refs.

Previous work has shown that the primary abnormality in this disease is in the erythrocytes themselves; the cells, or some of them, will undergo haemolysis when suspended in fresh serum from the patient or from normal subjects, provided that acid has been added to compensate for the alkalinity caused by loss of carbon dioxide when serum is exposed to air. This observation is the basis of an " acid haemolysis test " for the Marchiafava–Micheli syndrome. The author points out that for correct employment of this test specific steps must be taken to show that the haemolysis is not due to acidification alone. He shows that haemolysis can be increased by acidification in some cases of other haemolytic diseases unrelated to nocturnal haemoglobinuria. Haemolysis by abnormal " warm " and " cold " auto-haemagglutinins and pan-haemagglutinins may also cause confusion.

The author therefore suggests the following test. Four tubes are set up containing: (1) 10 volumes of normal fresh human serum and 1 volume of patient's erythrocytes in 50% saline suspension; (2) 10 volumes of normal serum acidified by adding 10% by volume of 0·2 N HCl, together with 1 volume 50% saline suspension of patient's cells; (3) 10 volumes of normal serum previously inactivated by heating to 56° C. for 30 minutes and then acidified as before, together with 1 volume 50% suspension of patient's erythrocytes; (4) 10 volumes of acidified *patient's* serum, together with 1 volume of 50% suspension of *normal* erythrocytes. Haemolysis should be considerable in tube 2, there should be at most only a trace in tube 1, and none at all in tubes 3 and 4.

It is also shown that the erythrocytes in nocturnal haemoglobinuria are unusually sensitive to anti-A and anti-B agglutinins when tested *in vitro* against these sera in the presence of complement from fresh guinea-pig or human serum. The erythrocytes are actually haemolysed, whereas normal cells are only agglutinated. Anti-Rh and anti-M sera did not show this phenomenon. Some evidence is quoted which suggests that the factor to which these erythrocytes are abnormally sensitive is distinct from complement and is present in normal serum. *M. C. G. Israëls*

2630. **Acquired Hemolytic Anemia. I. The Relation of Erythrocyte Antibody Production to Activity of the Disease. II. The Significance of Thrombocytopenia and Leukopenia**
R. S. EVANS and R. T. DUANE. *Blood* [*Blood*] **4**, 1196–1213, Nov., 1949. 2 figs., 24 refs.

It is now agreed that acquired haemolytic anaemia is caused by the action of a haemolysin. The destructive agent appears to be a globulin, since the erythrocytes are agglutinated by Coombs's anti-human serum rabbit serum. Like some Rh antibodies, the sensitized cells do not agglutinate in saline but require whole serum, 30% beef albumin, or 2% acacia in 1·5% calcium chloride. The sensitizing agent can be removed from the erythrocyte surface by heating a suspension of such cells at 56° C. in normal saline, and the authors have succeeded once in transferring the sensitizing body to normal erythrocytes.

In this paper they record attempts to devise a method of measuring quantitatively the amount of antibody on the erythrocyte and then relating the amount to the activity of the haemolytic process. They used as a measure the greatest dilution of antiglobulin (Coombs) serum to show agglutination, and showed that in an active phase of the disease titres of from 1 in 80 to 1 in 640 were obtained. In a quiescent phase titres were 1 in 1 to 1 in 20 and after splenectomy, although agglutination still occurred, titres were low (1 in 1 to 1 in 20), this corresponding with improvement in the blood state. Two of their patients had a spontaneous remission, without splenectomy, after a long period of activity and, coincidently, antiglobulin titres fell. But in another case apparently in remission the titre of antibody returned to high levels without any obvious return of haemolysis in the blood; no explanation is offered. Some evidence is also offered which suggests that destruction of granulocytes and blood platelets may, in some cases, be due to an immune-body reaction. Full details of techniques are given.

M. C. G. Israëls

Diseases of the Respiratory System

2631. **The Respiratory Response to Carbon Dioxide and Anoxia in Emphysema**
K. W. Donald and R. V. Christie. *Clinical Science* [*Clin. Sci.*] **8**, 33–44, 1949. 7 figs., 10 refs.

The respiratory response to inhalation of 4% carbon dioxide was studied in 23 cases of emphysema, 7 cases of asthma without emphysema, and 28 normal controls. The degree of bronchospasm was assessed by auscultation at rest, during attempted hyperventilation, and after exercise. Electrocardiograms and chest radiographs were taken and the plasma CO_2 combining power of venous blood determined. The vital capacity was measured with a Benedict spirometer.

The response to CO_2 was determined by a method described in *Clin. Sci.*, 1949, **8**, 21. The subject lay supine for 20 minutes, inhaled air for 6 minutes, and then inhaled 4% CO_2 for 5 minutes.

In 16 out of 23 cases of emphysema the increase in ventilation during exposure to 4% CO_2 was below the range in controls, the other 7 patients being those with the least degree of emphysema, and in most cases the least dyspnoea. The alkali reserve in all cases was normal. The impaired response to 4% CO_2 was shown not to be due to inability to increase tidal air or respiratory rate. The 7 patients with asthma all gave a normal response.

In 9 cases of severe emphysema the effect of exposure to 4% CO_2 for 12 to 14 minutes was also studied. In all but one case the increase in respiratory minute volume approximated to the normal at the end of this period. After this experiment the patients attempted hyperventilation with air, and 7 out of 9 achieved a normal increase in ventilation. Repetition of the above tests gave consistent results.

The effect of anoxia was shown to be similar in the normal and emphysematous subjects, but the latter reacted more slowly.

It is difficult to explain the impairment of response to 4% CO_2 in emphysema. The fault does not seem to lie with the blood buffers or the sensitivity of the respiratory centre, nor can mechanical limitation of chest movement be the cause. It is also difficult to believe that defective mixing of gases is a responsible factor.

S. S. B. Gilder

2632. **Reaction to Carbon Dioxide in Pneumokoniosis of Coalminers**
K. W. Donald. *Clinical Science* [*Clin. Sci.*] **8**, 45–52, 1949. 4 refs.

In view of the doubt about the part played by emphysema in causing disability in pneumoconiosis and the finding of impaired response to inhalation of 4% carbon dioxide in the former condition (see Abstract 2631), the authors studied the response of 56 coal-miners with pneumoconiosis to such inhalation. Tracings in 8 cases were unsatisfactory and were rejected.

Patients were placed in five groups according to the severity of dyspnoea. In group V, with dyspnoea at rest, 3 out of 4 showed impairment of response to 4% CO_2; 2 out of the 3 had no radiological evidence of pneumoconiosis, but only of severe emphysema. In group IV, with dyspnoea on slight exertion, 6 out of 11 gave an impaired response and 2 of these had minimal signs of pneumoconiosis, though all 6 had evidence of emphysema. Of the 5 with a normal response 4 had massive shadows in the radiograph. In group III only 3 out of 10, and in group II only 1 out of 19, had an impaired response, while all 4 with minimal dyspnoea (group I) gave normal reactions.

In 5 cases in which there was little evidence of pneumoconiosis but severe emphysema, response to CO_2 was very poor; in 11 out of the 13 with a poor response there was clinical and radiological evidence of emphysema, whereas in only 6 out of 34 with a normal response was there any such evidence. It is thus clear that the response is impaired only if true emphysema is present. It is also clear that severe dyspnoea may in this disease be associated with absence of emphysema and that the dyspnoea is in many cases not due to emphysema. Where emphysema is absent the degree of disability is not related to the severity of the pneumoconiotic lesions.

S. S. B. Gilder

2633. **What is Atelectasis?**
C. Xalabarder. *Tubercle* [*Tubercle, Lond.*] **30**, 266–283, Dec., 1949. 40 figs.

The author differentiates " atelectasis " from " collapse of the lung ", in that in the former there is intense retraction and shrinkage, while in the latter the alveolar walls are only flaccid and have not shrunk; in both conditions the alveoli contain little or no air. The phase of pure atelectasis is transient, the alveoli later being filled with an exudate whose nature depends on the pathogenesis of the atelectasis. It is argued that bronchial obstruction is not enough to produce atelectasis because: (1) it has been demonstrated by post-mortem bronchography that obstruction may occur without atelectasis; (2) bronchial obstruction is often not detected on bronchoscopy; (3) it has been shown post mortem that atelectatic lungs can be reinflated under a pressure of 14 cm. of water, but the retractile power of living lung may reach 30 to 40 cm. of water; (4) atelectasis is said only to be produced by obstruction of a main bronchus; its absence in the case of subsidiary bronchi has been attributed to collateral respiration, but the author does not accept this; (5) complete absorption of the gases in the atelectatic area is not to be expected unless their pressure is increased by active contraction of the lung. On thoracoscopy, atelectatic areas of the lung are seen to remain motionless during inspiration and their depression in relation to the surrounding parenchyma increases; their surface is

granular in appearance, and their clear-cut outline does not correspond to the position of normal fissures. Atelectatic areas are often multiple and irregularly dispersed, and vary greatly in size and shape. Sometimes in the middle of an otherwise atelectatic lobe there are " breathing zones ", which at thoracoscopy are seen to aerate with each inspiration; sometimes these zones are detectable in the radiograph. Atelectatic areas often appear in the region of the point stimulated by the cautery in unsuccessful adhesion section; the same principle underlies efforts to close large cavities, which have remained open in spite of artificial pneumothorax, by various forms of pleural stimulation. The author has produced small local areas of atelectasis by applying 1 in 1,000 acetylcholine to the visceral pleura. He also contends that temporary closure of cavities by Monaldi drainage is often due to local stimulation by the catheter and consequent atelectasis. The production of atelectasis by active contraction of the alveoli is brought about by plain muscle in the alveolar walls; several anatomists claim to have demonstrated the presence of such muscle.

[It is easy to criticize this paper in which an attempt has been made to assemble all available evidence in favour of atelectasis as an active process. Certainly many of the facts quoted are capable of other interpretations. The greatest value of the paper should lie in stimulating others to prove or disprove the theory. Since many authors are quoted, it is a pity that no references are given.]

John Crofton

2634. **Fibrosis of the Lungs Due to Infestation with *Oxyuris* (*Enterobius*) *vermicularis*.** (Parasitäre Lungenfibrose durch *Oxyuris* (*Enterobius*) *vermicularis*)
M. BRANDT. *Tuberkulosearzt* [*Tuberkulosearzt*] **3**, 685–688, Dec., 1949. 4 figs.

A case of chronic pulmonary fibrosis due to infestation of the lungs with immature eggs of *Oxyuris* (*Enterobius*) *vermicularis* had been diagnosed *in vivo* as a case of tuberculosis. Necropsy revealed fibrotic induration of both lungs; the spleen was enlarged, hard, and fibrotic; the left ovary was replaced by a hard tumour. Histologically both lungs showed in the hilar area multiple, miliary giant-cell granulomata (foreign-body granulomata), containing calcified, oval, shell-like, double-contoured bodies, 54·4μ × 23·8μ. These eggs were situated within fissures, simulating furrows. No specimen of *Oxyuris* was found. The spleen was infiltrated by similar giant-cell granulomata, and so was the ovarian tumour, but no eggs were found in these organs.

Two parasitologists independently made the diagnosis of immature eggs from *Oxyuris*, in spite of the impossibility of tracing their origin. The possibility of infestation by aspiration from the mouth was dismissed. The finding of old granulomata as well as of " fresh " (immature) eggs would point to repeated aspiration, which is unlikely. The possibility of inhalation of eggs in dust was also rejected. The chance that some worms perforated the intestine and were carried in the lymph or the blood stream to the lungs is thought to be more likely. [Here again it is difficult to account for the apparent absence of the female parasite. As the disease, however, was present at least 6 years before death the following course of events appears feasible. The deposition of eggs had taken place some 6 years before death. The one or two female worms which originally reached the lung were destroyed by some degenerative process (? enzyme digestion). Their remains were absorbed, while the hard and resistant eggs remained in their original shape and size.] *E. G. W. Hoffstaedt*

2635. **South-West Pacific Pulmonary Disease**
B. THOMPSON. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **53**, 1–5, Jan., 1950. 22 refs.

The author describes a peculiar type of pulmonary fibrosis, probably non-tuberculous, which is common in Western Samoa. Radiologically the lesion varies from an increase in the bronchovascular markings, without gross distortion, heaviest towards the lung base and with increased density at the hilum, to a definite fibrosis radiating from the hilum with contraction of the vessel markings, sometimes with mediastinal displacement and pleural involvement. The appearances suggest interstitial rather than parenchymatous disease, and are quite unlike those of silicosis or miliary tuberculosis. Calcification and cavity formation are absent. Clinically the symptoms are indistinguishable from those of pulmonary tuberculosis. The resemblance to pulmonary tuberculosis is discussed, but the negative bacteriological findings and basal distribution of the lesions differentiate the condition from tuberculosis. Clubbing of the fingers and bronchiectasis are absent. [Unfortunately there were no post-mortem studies.] The author discusses the relation of these lesions to helminth infestation, which is rife among the islanders. He also comments on the extremely chronic course of pulmonary tuberculosis in the Samoan native.

Maxwell Telling

2636. **Lung Function Studies. III. Uneven Pulmonary Ventilation in Normal Subjects and in Patients with Pulmonary Disease**
W. S. FOWLER. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 283–299, Dec., 1949. 3 figs., 18 refs.

Not being satisfied with the theory of " stratification " or with the " regional " concept of uneven lung ventilation, the author reinvestigated the problem with a view to obtaining quantitative data on the lack of uniformity of alveolar gas. Pulmonary ventilation was studied in normal subjects and in patients with bronchial asthma and emphysema.

The practical outcome of this work was the introduction of the " uniformity index " for the measurement of intrapulmonary gas mixing, the normal value being 0·725 (it expresses the minimal variation in dilution of alveolar nitrogen by inspired oxygen). The index has been calculated for a group of healthy individuals and may serve to identify abnormal intrapulmonary gas mixing in patients with cardiopulmonary disease. The method is described in detail.

The results of his experiments lead the author to formulate the " sequential ventilation " theory to explain uneven lung ventilation. This is based on the fact that certain areas of the lung fill mainly during the first part

of inspiration; these areas will receive more of the dead-space gas and less oxygen than the areas which fill later. Thus regional differences in alveolar gas composition arise towards the end of inspiration even though the final percentage increase in volume of gas is equal in all areas. Continuous analyses of the expired air indicated that there was also sequential emptying. Sufferers from bronchial asthma and pulmonary emphysema showed greater variations in alveolar gas composition than did healthy subjects. *A. I. Suchett-Kaye*

2637. **The Reserve Air as an Aid in the Diagnosis of Emphysema**
H. HERXHEIMER. *Thorax* [*Thorax*] **4**, 73–81, June, 1949. 6 figs., 15 refs.

The author found, in a group of 46 emphysematous patients whose vital capacity was normal or above normal limits, that 43 had an increase in reserve air (49% of the vital capacity). The corresponding value in 48 normal controls was 33% of the vital capacity.

In another group of 77 emphysematous patients whose vital capacity was subnormal the reserve air was frequently found to be normal. In some of these, antispasmodic drugs "unmasked" a large reserve air, suggesting that bronchial spasm was causing incorporation of a proportion of a potentially large reserve air within the residual air.

[In all these determinations the latter component was not investigated, a fact which, in the abstracter's opinion, largely detracts from the significance of the findings, and which almost certainly invalidates the conclusion that an increased reserve air is a useful diagnostic sign in emphysema.] *W. D. W. Brooks*

2638. **Experimental and Clinical Studies of the Role of Streptomycin in the Pleural Cavity**
E. J. BEATTIE, B. BLADES, and C. HORTON. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **18**, 25–35 and 55–63, Feb., 1949. 15 figs., 8 refs.

See also Section Hygiene and Public Health, Abstract 2369.

PULMONARY INFECTIONS

2639. **Aureomycin Therapy in the Pulmonary Involvement of Pancreatic Fibrosis (Mucoviscidosis)**
H. SHWACHMAN, A. C. CROCKER, G. E. FOLEY, and P. R. PATTERSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **241**, 185–192, Aug. 4, 1949. 4 figs., 34 refs.

The authors report the treatment of 35 patients with fibrocystic disease of the pancreas and pulmonary involvement with aureomycin by the oral route in a dose of 20 to 30 mg. per kg. body weight. They investigated the bacterial flora of the upper respiratory tract in each case and found that *Haemophilus influenzae* and *Staphylococcus aureus* were the most sensitive to aureomycin of the species included in the series. Of the strains of *Staph. aureus* tested, the majority were relatively more sensitive to aureomycin than to penicillin or streptomycin. Most of the patients had previously received penicillin or streptomycin, or both.

The most striking effect of aureomycin therapy was the consistent amelioration of cough, dyspnoea, and respiratory distress, response beginning usually in 2 or 3 days. Clinical improvement bore no relation to bacteriological improvement, the former being commonly, and the latter only rarely, observed. On discontinuing the aureomycin relapse occurred within 3 to 7 days. The *Staph. aureus* isolated from 7 patients during aureomycin therapy showed an apparent increase in resistance varying from 4-fold to 32-fold. These patients, however, continued to show clinical improvement on the same dosage schedule. *Patrick Mallam*

2640. **Treatment of Primary Atypical Pneumonia with Aureomycin**
H. S. COLLINS, E. B. WELLS, T. M. GOCKE, and M. FINLAND. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 4–20, Jan., 1950. 8 figs., 17 refs.

Thirty-two patients with primary atypical pneumonia were treated with aureomycin by mouth, the usual dose being 1 g. every 4 to 6 hours, continued until an average total dose of 10 to 12 g. had been given. The diagnosis was made on clinical, radiological, and laboratory findings, the presence of cold agglutinins being demonstrated in every case. It was not possible to provide a control series of cases, but comparison is made with 8 patients with a similar illness, but in whom no cold agglutinins could be demonstrated, and with 9 patients with acute non-specific pulmonary infections in whom the diagnosis of primary atypical pneumonia was, for various reasons, rejected. Tests for psittacosis, Q fever, and influenza were negative in all patients.

In every case of proved primary atypical pneumonia symptomatic improvement after aureomycin administration started was rapid and striking. In most cases the temperature fell to normal within 48 hours. In many patients the response to treatment is described as "dramatic". Radiological clearing of the lungs was less rapid, but in more than half the cases the lungs were clear in 10 days. Similar results were obtained in the second group of 8 cases, thought to be cases of primary atypical pneumonia despite the apparent absence of cold agglutinins.

The other 9 cases of acute non-specific pulmonary infections are discussed in detail. In no case was the response to aureomycin striking, though one or two cases in which it was thought that possibly the virus of primary atypical pneumonia, or perhaps a mixed bacterial flora, might have played a contributory part did show some improvement.

It is concluded from this series of cases that the evidence for the beneficial action of aureomycin in primary atypical pneumonia, though not entirely conclusive, is nevertheless convincing.

The only untoward effects of the drug were nausea and vomiting in about half the cases. In only 4 patients were these symptoms severe enough to require its discontinuation. *John Forbes*

2641. **Aureomycin in the Treatment of Influenza and Certain Other Acute Respiratory Infections with or without Pneumonia**
M. FINLAND, E. B. WELLS, H. S. COLLINS, and T. M. GOCKE. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 21–30, Jan., 1950. 14 refs.

This is a parallel study to that in the previous article (Abstract 2640). Aureomycin was used in the treatment of a miscellaneous group of 41 cases of acute severe respiratory infection with or without evidence of pneumonia.

In 18 cases of serologically proved influenza-A infection rapid improvement was obtained similar to that observed in primary atypical and bacterial pneumonias. The authors consider, however, that, in view of the absence of previous experimental evidence of the efficacy of aureomycin against the influenza viruses, the beneficial results may have been due to the drug's action on secondary invaders. Equally rapid improvement was observed in other cases of clinically similar infections (though without serological evidence of influenza) and in cases of lobar pneumonia.

[The value of such uncontrolled and somewhat diffuse studies of disorders known to be self-curing in the majority of instances seems doubtful, though the difficulties of virus identification do not make the task of careful clinical evaluation easy. However, there seems now to be a considerable body of evidence of the value of aureomycin in primary atypical pneumonia. Its action against influenzal infections seems less definite.]

John Forbes

See also Section Hygiene and Public Health, Abstract 2364.

TUMOURS

2642. **The Fate of Oil Particles in the Lung and their Possible Relationship to the Development of Bronchiogenic Carcinoma**
L. R. SANTE. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **62**, 788–797, Dec., 1949. 6 figs., 24 refs.

Highly refined vegetable oils free from fatty acids are removed from the alveoli by phagocytic action, and this leads eventually to complete removal without evidence of damage to the lung structures. Oil that has deteriorated should not be injected into the bronchial tree because of the possibility that fatty acids may be present. A change in colour of the oil is evidence of deterioration.

Animal oils contain a high percentage of fatty acids, and are thus in themselves irritant. Further, they remain longer in the alveoli and even larger amounts of fatty acids are formed. As a result lipoid pneumonia develops and may be fatal.

Mineral oils are also removed from the alveoli by the action of phagocytic cells but, being inert, they cannot readily be autolysed by the cells and are carried with little change through the regional lymphatics to the hilum, where they excite an extreme degree of cellular reaction which results in fibrosis and scarring. The phagocytic cells themselves are often destroyed by the oil which they contain. The resultant mass of paraffin-oil droplets enmeshed in heavy scar tissue gives rise to a paraffinoma. Paraffinomata may attain several centimetres in diameter and are usually found about the large bronchial branches near the root of the lung at the site of the hilar lymph nodes.

The author discusses the possibility of carcinomatous change supervening in the paraffinomata and quotes two cases in which this seems to have occurred. [The second case quoted is less convincing in that the lipoid change is distal to a primary bronchial carcinoma. It is well known that such change may occur in the absence of any history of inhalation of oil.] *L. G. Blair*

2643. **Conditions for the Development of Cancer of the Lung.** (Ontstaansvoorwaarden voor longkanker)
W. F. WASSINK. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **92**, 3732–3747, Nov. 13, 1948. 3 figs., 32 refs.

A study of 143 cases of pulmonary cancer, 136 in men and 7 in women, was made from the points of view of occupation and tobacco-addiction. This form of cancer was found to occur chiefly among intellectuals and white-collar workers and seldom in agricultural workers. This group showed the highest degree of tobacco-addiction found among cancer sufferers. Similar but less definite figures were found for cases of endolaryngeal cancer. It is concluded that smoking and the inhalation of smoke-laden air constitute the foremost exogenous causal factors in the incidence of pulmonary cancer in men in the Netherlands.

A. Schaberg (Excerpta Medica)

2644. **The Early Cytological Diagnosis of Bronchial Carcinoma by Means of Bronchial Catheterization.** (Zytologische Frühdiagnose des Bronchialkarzinoms mit Hilfe der gezielten Bronchialsonde)
H. HENGSTMANN and D. WITTEKIND. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **75**, 101–104, Jan. 20, 1950. 8 figs., 12 refs.

A method of obtaining specimens of secretion by means of bronchial catheterization is described. [The method of catheterization appears to be inferior to that originated by Métras and Lieutier, *Thorax*, 1947, **2**, 196.]

The findings in 21 cases of suspected carcinoma of the bronchus are discussed. In only 7 was the diagnosis confirmed histologically. Definite tumour cells were recognized in 17, and in a further 2 cases doubtfully malignant cells were seen. In 2 no tumour cells were found. Three specimens contained fragments of tumour sufficiently large to be sectioned. Sputum was available in 16 cases; only in 7 were neoplastic cells seen. Catheterization is useful for the early diagnosis of peripherally situated tumours and those in the upper lobes.

[Some pathologists consider that the incidence of false-positive reports on specimens obtained by procedures involving intrabronchial trauma is so high that it is better not to use these methods at all.] *J. R. Bignall*

Digestive Disorders

2645. **A Contribution to the Knowledge of Banti's Syndrome. With Special Emphasis on Differential Diagnosis and Treatment.** [In English]
L. E. CARLGREN, A. LICHTENSTEIN, and P. H. SANDBLOM. *Acta Paediatrica* [*Acta paediatr., Stockh.*] Suppl. 75, 10–56, 1949. 32 refs.

This paper consists of an excellent survey of the known facts and theories of the complex problem of Banti's syndrome, supplemented by a study of the symptoms and treatment in 14 of the authors' own cases. It is concluded that until more is known of the disease the syndrome is best divided into three types: (1) splenomegalic hepatic cirrhosis; (2) cases in which the damage seems to have affected particularly the portal vein and its tributaries; (3) idiopathic enlargement of the spleen. Type (3) is thought to be so rare that it can be disregarded, and the authors' cases are divided into equal numbers of types (1) and (2).

In the differential diagnosis stress is laid on the finding of icterus, urobilinuria, increased prothrombin time, and a raised erythrocyte sedimentation rate in type (1); all these findings are uncommon in type (2), in which oesophageal varices and haematemeses are important features. In general, type (1) occurs in older children and has an insidious onset; type (2) is more sudden in onset and occurs in a younger age group. Anaemia, leucopenia, thrombocytopenia, and ascites are common to both groups, and liver function tests are of little help in the differential diagnosis.

Surgical treatment is advocated only in type (2), and here the important finding is that splenectomy alone is disappointing. It should be accompanied at the same operation by an anastomosis (preferably spleno-renal) between the portal and systemic systems. Anastomosis performed at an interval after splenectomy was found to be unsatisfactory because the portal system became sclerotic with a vein lumen so narrowed that the " shunt " was not maintained. *N. M. Jacoby*

2646. **Chronic Pancreatitis and Lithiasis. I. A Clinicopathologic Study of 62 Cases of Chronic Pancreatitis**
H. A. EDMONSON, W. K. BULLOCK, and J. W. MEHL. *American Journal of Pathology* [*Amer. J. Path.*] **25**, 1227–1247, Nov., 1949. 11 figs., 37 refs.

This paper describes the clinical and pathological findings in 62 cases of chronic pancreatitis which occurred among 33,500 necropsies (0·18%). Pancreatic changes secondary to perforating peptic ulcer and duct obstruction by cancer were excluded. Only in 3 cases was jaundice present. There was no constant change in the size of the pancreas; in severe cases it was nodular and hard to cut, but the condition was not always diagnosed macroscopically. Microscopically, acute necrosis (present in 16 cases) occurred particularly towards the periphery of a lobule and was followed by connective-tissue replacement. Dilated ducts with hyperplastic epithelium were seen frequently, but there was no obstruction to account for this finding. Very small calculi were found only once. The incidence of alcoholism (38·7%) was striking, and in some of these cases portal cirrhosis was also present. A history typical of pancreatitis was found in only 4 cases.

Brian E. Heard

2647. **Peripheral Pain in Chronic Pancreatitis.** (Periphere pijnen bij chronische pancreatitis)
L. A. HULST. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 3126–3131, Sept. 10, 1949. 4 refs.

Three cases of chronic pancreatitis are discussed, chiefly in connexion with the nature and varying localization of the pain. Sympathectomy was performed in 2 cases and led to disappearance of the colic but not of the peripheral pain. *S. Lups* (*Excerpta Medica*)

2648. **Functioning Pancreatic Islet Cell Adenomas. A Review of the Literature and Presentation of Two New Differential Tests**
E. L. CRAIN and G. W. THORN. *Medicine* [*Medicine, Baltimore*] **28**, 427–447, Dec., 1949. 5 figs., bibliography.

2649. **Fibrosis of the Pancreas. Enterogastrone and the " Duodenal Mechanism " in Relation to Increased Appetite**
C. U. LOWE, C. D. MAY, H. M. STAUFFER, and E. D. B. NEUHAUSER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 91–98, Jan., 1950. 3 figs., 23 refs.

2650. **Treatment of Ulcerative Colitis with a Fractional Component of Hog Stomach Extract**
R. EHRLICH. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **17**, 1–4, Jan., 1950. 4 refs.

2651. **The Role of Fat Ingested in the Diet in the Incidence of Sprue**
J. C. GILROY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **43**, 303–310, Nov., 1949. 14 refs.

The high incidence of sprue amongst troops in India and the Far East during the last war was in striking contrast to its absence in prisoners of war in Japanese hands. The numbers discharged each year from the British Army as unfit for further military duties owing to sprue were 6, 49, 196, and 73 for the years 1943–6 inclusive. Out of 8,000 men invalided home from the Far East on medical grounds during 1944 and 1945, 1,000 were cases of sprue. Yet among 127 released prisoners of war examined by the author there was not a

single case of sprue, nor did any of them develop sprue on returning to a more normal diet. These findings are similar to those made by other observers. The significance of these differences in relation to the aetiology of sprue is discussed, the possible importance of dietary factors being emphasized. *A. C. Frazer*

OESOPHAGUS

2652. **A Study of the Effect of Certain Drugs on Curling of the Esophagus. A Preliminary Report**
A. SHEINMEL, C. A. PRIVITERI, and M. H. POPPEL. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **62**, 807–813, Dec., 1949. 4 figs., 20 refs.

The term "curling" or "crenation" (*Kräuselung*) was introduced by Schatzki in 1933 to describe multiple irregular localized contractions and dilatations of the oesophagus. These are due to incoordinated muscle spasms which do not usually encircle the oesophagus, but tend to occur on the anterior, lateral, and posterior walls from the level of the aortic arch downwards. [The so-called "corkscrew" oesophagus results from a more or less regular distribution of these spasms.] The condition has been neglected except by radiologists. The contractions are best shown in films with the patient horizontal and the oesophagus filled with barium. The contractions may be persistent or evanescent, but there is no progression as with peristaltic waves. The relation between curling and other pathological conditions is uncertain. [There is some connexion with achalasia; achalasia has several times been observed to follow curling after an interval of months or years; or achalasia and curling may alternate at first.]

The condition is rare, but the authors claim to have seen 15 cases in 18 months. In 13 no symptoms could be ascribed to the oesophagus. In 2 oesophageal pain paralleled the degree of curling. It was found that administration of amyl nitrite and amphetamine completely eliminated curling and the symptoms. The effect of the amyl nitrite lasted for only a minute or two; that of the amphetamine was "more lasting". In one patient there was almost complete relief after taking 15 minims (0·9 ml.) tincture of belladonna 3 times a day or after an injection of $\frac{1}{100}$ grain (0·65 mg.) atropine 4-hourly. In another patient these two preparations had only a slight effect. [The response of the remaining patients was not tested.] *Denys Jennings*

2653. **The Short Oesophagus. A Review of 31 Cases**
J. B. RENNIE, F. T. LAND, and S. D. SCOTT PARK. *British Medical Journal* [*Brit. med. J.*] **2**, 1443–1449, Dec. 24, 1949. 3 figs., 28 refs.

This article, which starts with a brief historical review of the literature, describes the clinical features of the short oesophagus associated with hiatus hernia of the diaphragm, based on 31 cases admitted to the Western Infirmary, Glasgow, from 1937 to 1946. Dysphagia was complained of by 26 patients. During the same period, in 80 cases carcinoma was responsible for this symptom, and in 31 achalasia. Eighteen patients complained of burning pain, usually at the lower end of the sternum, radiating upwards and to the back; most commonly felt on swallowing, it was sometimes delayed and was mostly relieved by passage or regurgitation of food. In 9 cases there was haematemesis; in 4 it was gross, but in only one case was there anaemia. Symptoms were characteristically intermittent.

For accurate radiological examination, a barium swallow must be given with the patient first standing and then tilted. In 26 patients a simple stricture was found, and in 15 an oesophageal ulcer. At oesophagoscopy, oesophagitis, sometimes with granulations or shallow ulcers, was seen about 2·5 cm. proximal to the stricture, which might be due to fibrosis or spasm.

One patient had a carcinoma in a thoracic stomach. Seven patients had a history of gastric or duodenal ulceration. Three patients first developed dysphagia within a few days of a laparotomy. In 5 patients oesophageal symptoms began in the later months of pregnancy, and were not preceded by vomiting. It is suggested that the increased intra-abdominal pressure caused gastric reflux through an incompetent cardia.

There is little information on pathology available. In one of the patients, dying from another cause, at necropsy the oesophagus was not found to be short, but the hiatus was large (5 cm. wide). The initial lesion is thought to be a weakness of the hiatal ring, allowing herniation and reflux of gastric juice into the gullet. The resulting shortening may be due to spasm or to cicatrization.

Most of these patients led a reasonably comfortable life if they were careful about diet and if bougies were occasionally passed. *M. Meredith Brown*

2654. **Clinical and Roentgenologic Aspects of Esophageal Lesions in Scleroderma. Report of Six Cases**
A. M. KAISCH. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **16**, 405–413, Nov., 1949. 2 figs., 26 refs.

The author reports 6 cases of scleroderma, with sclerodactyly in every case, in which the skin lesions had been present for periods ranging from 9 months to 25 years. Of the 6 patients 3 complained of epigastric distress and heartburn, 1 of difficulty in swallowing, and 2 had no complaints referable to the oesophagus. Gastrointestinal symptoms were subordinate in all. *X*-ray examinations were performed in 5 cases, in which the radiographs of the oesophagus [which are not reproduced] are said to have shown dilatation, elongation, rigidity, or narrowing—usually with loss of peristalsis, but no marked delay at the cardia. Necropsy was performed in 2 cases. In one there was considerable thickening of the collagen fibres in the oesophagus and stomach, with multiple ulcers of the oesophagus and a duodenal ulcer involving the mucosa and submucosa. In the other, chronic oesophagitis was complicated by secondary neoplastic invasion, the primary site being unknown. A test meal was performed in only 1 case of the series, free acidity being 80 units. The general nature of scleroderma is discussed and it is pointed out that other conditions may complicate it. Oesophageal symptoms are attributed either to regurgitation of gastric acid or to

an oesophagitis analogous to the atrophic changes in sclerodermatous skin. No treatment of the oesophageal condition was attempted in what were evidently advanced cases.

[The appearances here attributed to scleroderma of the oesophagus can be matched by those due to peptic inflammation or ulcer, but appear also in occasional achlorhydric patients or in cases of neoplasm. Sclerosis of the oesophagus probably presents a similar appearance whatever the cause, peptic ulceration being the commonest, although scleroderma may also be responsible. Sclerodactyly or Raynaud's phenomenon is a practically invariable concomitant of scleroderma, as in these cases, and because of its progressive and grave nature should be inquired into before surgical measures are undertaken.] *W. A. Bourne*

STOMACH

2655. **Difficulties in the Diagnosis of Carcinoma of the Upper Pole of the Stomach.** (Difficultés dans le diagnostic du cancer du fornix)
E. VIDAL-COLOMER and J. BADOSA-GASPAR. *Gastroenterologia* [*Gastroenterologia, Basel*] **75**, 1–8, 1949. 9 figs.

Three cases are described, and there is a brief review of the literature on this type of carcinoma (which originates above the cardia but obstructs it late or not at all and is therefore difficult to diagnose). Some tumours are slow-growing, and there may be a history of vague digestive discomfort for several years. Often the neoplasm is completely silent, and an extensive lesion is found when an unexpected haemorrhage leads to full investigation. At the onset, however, there may be only vague ill-health and anaemia which may, or may not, be associated with indigestion. A few patients give a history of isolated attacks of severe pain in the left hypochondrium, or radiating into the left chest. In this group the diagnosis may be missed at first, the patient being referred to a cardiologist. When pain is regularly related to meals, the interval is usually short so that food intake is severely restricted and there is rapid weight loss. In most cases weight loss is a late symptom.

As with carcinomata of the greater curve, histamine achlorhydria is usual. Radiological diagnosis is difficult and mistakes are common. Even when the radiologist's attention is specially directed to this area, a dogmatic opinion may be impossible. Good radiographs with the patient in the erect position are essential; these often show the tumour shadow encroaching on the gastric air bubble. [A Seidlitz powder often helps by distending the upper pole of the stomach.] Films taken with the patient prone and supine tend to be less helpful. Gastroscopy usually enables an exact diagnosis to be made, and four colour plates illustrate this.

[Two further points are worth adding. Gastroscopy may cause perforation if soft neoplasm has invaded the posterior wall just below the cardia. In some cases in which it is impossible to make the gastroscope pass through the cardia, a hard resistance is felt which is almost pathognomonic of cancer.] *Denys Jennings*

2656. **The Uptake of Radioactive Phosphorus by Gastric Carcinoma in the Human**
S. J. GRAY, J. SCHULMAN, and M. FALKENHEIM. *Gastroenterology* [*Gastroenterology*] **13**, 501–512, Dec., 1949.

A dose of radioactive phosphorus (1 microcurie per lb. (0·45 kg.) body weight) was administered intravenously 36 hours before gastrectomy for carcinoma in 4 cases and ulcer in 6. One hour after resection the rate of turnover of radioactive phosphorus and the phosphorus content (total, acid-soluble, lipid, and protein fractions) were measured in different parts of the stomach. In the stomachs without carcinoma there was no difference as regards these values between those areas in which cancer commonly occurs and those in which it does not. Atrophic gastric mucosa also metabolized phosphorus normally.

Although cancerous tissue itself showed an increase in the rate of turnover of the radioactive phosphorus, the increase was not demonstrable in the surrounding tissues. The actual phosphorus content of the cancerous and the normal mucosa was found to be essentially the same. The rate of turnover of total phosphorus in the cancer tissue was 48·5% higher than in normal mucosa; that of the protein phosphorus was increased by 126%, and that of the lipid phosphorus by 48·5%. There was no change in the acid-soluble fraction. *John Naish*

2657. **Studies of Gastric Acidity by Direct Estimation of the Gastric *p*H.** (Studien über die HCl-Sekretion des Magens mit der pH-Sonde)
H. KREITNER and M. PANTLITSCHKO. *Wiener Zeitschrift für Innere Medizin* [*Wien. Z. inn. Med.*] **30**, 443–448, Nov., 1949. 2 figs., 10 refs.

The details of the indwelling gastric electrode employed by the authors have been described elsewhere (*Wien. Z. inn. Med.*, 1949, **30**, 160). The two main advantages of its use consist in the direct measurement of gastric *p*H and in the obviation of any effect that aspiration of gastric juice might have on gastric secretion. Healthy subjects and patients with duodenal ulcer, gastric ulcer, and gastric carcinoma were investigated.. Fasting values of gastric acidity and the response to injection of 1 mg. of histamine over a 2-hour period were estimated.

In the healthy subjects resting values of *p*H were mostly between 7 and 6, the peak values of 2 to 1·5 were reached within 60 minutes, and the initial values regained after a further 40 to 60 minutes. In the cases of duodenal ulcer resting values ranged from 2·5 to 2. The peak value of 1·5 was reached within 20 to 45 minutes and the return to initial values occurred after a further 20 to 40 minutes. After vagotomy 4 out of 5 patients had free acid in the resting juice 10 days after the operation, but this had disappeared at a further test 6 months later in all cases. Of the 10 cases of gastric ulcer 3 showed normal values and 7 had hyperchlorhydria. In gastric carcinoma the resting *p*H was about 8 and histamine injection only produced a brief rise to 7. The effect of a teaspoonful of an antacid powder on the *p*H of a duodenal ulcer patient only lasted for 40 minutes, and the effect of 20 drops of dilute hydrochloric acid in a case of achlorhydria for 12 minutes. *R. Schneider*

2658. **Nitrogen Mustard in the Therapy and Prophylaxis of Chronic Gastric Ulcer.** (Chlorethylaminy (TS 160) v léčbě a prevenci chronických žaludečních vředů) O. Soušek and V. Beck. *Časopis Lékařů Českých* [*Čas. Lék. čes.*] **88**, 1372–1376, Nov. 25, 1949. 11 refs.

In this preliminary report the authors describe the effect of nitrogen mustard in the treatment of 12 cases of chronic fibrous gastric ulcer.

The basis of their treatment was the observation that after injection of nitrogen mustard into other patients the acidity of the gastric juice decreased, indicating a pharmacological action of nitrogen mustard desirable in the treatment of chronic gastric ulcer. In addition, they ascertained that after initial dyspeptic disturbances during treatment with nitrogen mustard, appetite improves, persistent pain is alleviated, and patients are often in a state of complete euphoria. The authors selected for their trial cases with a long history of gastric ulcer, the diagnosis of which was confirmed by gastroscopy; the latter method was used to demonstrate the local changes after treatment with nitrogen mustard. During treatment, the blood picture and erythrocyte sedimentation rate were studied at intervals. The treatment consisted of a total of 4 injections, the dose depending on the patient's weight. Patients were kept on a light diet with restriction on smoking. The authors conclude that, apart from the known effect of nitrogen mustard on haematopoietic organs, there is a noticeable depressive effect on the secretion of gastric juice; symptoms such as pain, dyspepsia, and constipation diminish or disappear. Cure in 7 cases, after small doses given in 4 injections, justifies further trial of the therapy with nitrogen mustard.

In addition, the authors suggest that repeated injections of small doses of nitrogen mustard may be used to prevent recurrence of gastric ulcer by keeping gastric secretion low.

J. Ungar

2659. **Gastric Ulcers in the Aged**
E. Levin, J. B. Kirsner, and W. L. Palmer. *Geriatrics* [*Geriatrics*] **4**, 362–373, Nov.–Dec., 1949. 9 refs.

Of the 450 patients with benign gastric ulcer seen at the University of Chicago clinics since 1936, 41 (11%) were over the age of 65. These elderly patients form the subject of this paper.

The difficulty in distinguishing between benign ulcer and cancer of the stomach is strongly emphasized. Symptoms of gastric ulcer were frequently misleading: loss of weight (often severe) occurred in two-thirds, anorexia in one-quarter, pain unrelated to food in one-third, and there was a history of under 6 months' symptoms in one-quarter. Ancillary methods of diagnosis often gave misleading results; an initial misdiagnosis of cancer was made radiologically in 11 cases and by gastroscopy in 2 cases. The correct diagnosis was made only after resection in 6 cases and at necropsy in 1 case.

The rate of healing as determined objectively by radiological and gastroscopic examination was slower in the elderly than in younger patients. Complications were more frequent, occurring in 68% of this series; haemorrhage in 44%, with one death, obstruction in 15%, and alkalosis in 17%. Malignant change and perforation did not occur.

The indications for surgery were much the same as in the young, including perforation, inability to distinguish a benign from a malignant ulcer, persistent pyloric obstruction, and uncontrollable haemorrhage. Medical management was preferred, even for frequent recurrences, where conditions were such as to allow frequent gastroscopic and radiological examinations. Medical management included rest in bed, diet, and administration of antacids and atropine. Alkalosis was corrected by giving physiological saline and 10% ammonium chloride. For haemorrhage blood transfusions were required. In 11 cases irradiation with *x* rays was used in an endeavour to reduce gastric secretion. In all, a reduction in acid secretion occurred. Nine of these cases responded to medical treatment and 2 required surgery. Of 32 patients treated medically 12 had one or more recurrences. Of the 27 treated by medical management alone 4 died: 1 of haemorrhage, 1 of cancer of the uterine cervix, 1 of heart failure, and 1 of an undetermined cause. Fourteen patients were treated surgically. The results of vagotomy were poor, those of partial gastrectomy (10 cases with 2 deaths) satisfactory.

P. D. Bedford

2660. **Neuro-humoral Factors in Pathogenesis of Peptic Ulcer.** (Нейрогуморальные факторы патогенеза язвенной болезни)
R. I. Sharlai. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 11, 60–64, Nov., 1949. 8 refs.

During the war the incidence of peptic ulcer in the Red Army increased 2 to 3 times (Stewart and Winser, *Lancet*, 1942, **1**, 259). This fact led to the initiation of the present work, involving the investigation of 438 patients, 84 with malignant neoplasms of the stomach and the rest with peptic ulcer. Of these 168 patients underwent gastric resection.

Blood and cerebrospinal fluid were tested for cholinergic activity with eserinized leech muscle. In 76% of the patients the blood from the antecubital vein showed cholinergic activity; when this blood did not give the reaction it was always possible to obtain a positive result with blood from gastric veins. The cerebrospinal fluid contained acetylcholine in 92% of the cases. After gastric resection the acetylcholine reaction became negative within 10 to 15 days. The following conclusions were reached. (1) In these cases blood from the gastric veins contains more acetylcholine than does the cerebrospinal fluid, and much more than blood from the antecubital vein. (2) Cholinesterase increases *pari passu* with acetylcholine in blood. (3) When acetylcholine is present the colour reaction for adrenaline is unobtainable. (4) Usually the alkali reserve is lowered when acetylcholine is found in the blood. (5) With acetylcholine present in the blood and a lowered alkali reserve, the amount of potassium ion and the erythrocyte sedimentation rate are raised, as usually are the gastric acidity and amount of polypeptides in blood. (6) The blood sugar concentration is raised when acetylcholine is present, the two increasing concomitantly. (7) The leucocyte

count is usually lowered, but this fall is unrelated to the strength of the acetylcholine reaction.

[The value of these conclusions would be greater in the presence of the data from which they are derived. Many of the phenomena are explicable in terms of acidosis arising from gastric hyperacidity. This work lends additional interest to the theoretical aspect of vagotomy.]

Jeffrey Boss

2661. **Peptic Ulcer Cases Reviewed after Ten Years. Effect of Medical Treatment and Indications for Gastrectomy**

L. MARTIN and N. LEWIS. *Lancet* [*Lancet*] **2**, 1115–1120, Dec. 17, 1949. 10 refs.

During the 5 years 1934–8 inclusive, 356 cases of peptic ulcer were admitted to Addenbrooke's Hospital, Cambridge, and most of the patients were treated in the medical wards. The cases were reviewed in 1948–9. In every instance the presence of an ulcer was confirmed either by radiological examination or at operation or necropsy. A history of ulcer dyspepsia during the 5 years before the year of review was regarded as the criterion of activity. Peptic ulceration was the cause of death in 75 cases and active ulceration was present in 23 patients who died from other diseases. There were 99 cases of haemorrhage, with 14 deaths, and 101 cases of perforation, with 36 deaths. The highest mortality rate was in elderly patients. Approximately 55% of haemorrhages and 45% of perforations occurred in cases with a history of peptic-ulcer activity for a period of at least 10 years. Six patients died from gastric carcinoma, but in no case was there any indication that the disease had originated from a peptic ulcer.

Apparently, medical treatment was successful in 42 of 96 cases of gastric ulcer and in 14 of 43 cases of duodenal ulcer. These statistics are in accordance with the findings of Heuer, who considers that medical treatment is unlikely to succeed in more than 50% of patients admitted to hospital (Heuer, *Treatment of Peptic Ulcer*, Philadelphia, 1944). Medical treatment may prove effective in relieving discomfort when a relapse occurs, but there is every indication that it fails to affect the natural course of the disease and that prolongation of the course of treatment increases the chances of failure. Surgical treatment is to be preferred when peptic ulceration persists for 10 years or longer, and especially when the patient is less than 50 years of age. Gastrectomy is the operation of choice. Admittedly the operation has a mortality rate ranging from 5 to 15%. Nevertheless, if surgical intervention is withheld, the patient faces the risk of haemorrhage, perforation, or malignant neoplasm.

A. Garland

2662. **The Insulin Test for Vagal Section**

B. N. BROOKE. *Lancet* [*Lancet*] **2**, 1167–1170, Dec. 24, 1949. 4 figs., 8 refs.

This paper is a plea for standardization of technique in the insulin test, used post-operatively to demonstrate inadvertent incomplete vagus resection.

Evidence is adduced to show that the blood sugar level must be lowered to 40 to 45 mg. per 100 ml. to ensure adequate stimulation. It was found that before operation, or 6 months after incomplete vagotomy, a positive response occurred in 82% of cases when an intravenous dose of 10 units of insulin was given.

Many patients in whom no gastric acid was secreted in response to insulin one month after operation gave positive results when tested again 6 months later. A standard test is proposed in which 10 units of insulin are given 6 months after operation and blood sugar level is estimated 30 minutes after the injection.

[Dragstedt (*Arch. Surg.*, 1949, **59**, 1191) employs 20 units, and the abstracter, as he has reported to the Royal Society of Medicine, uses 1·25 units per stone (6·3 kg.) body weight, with 10% of failures in the controls. It is doubtful whether 10 units of insulin will be widely accepted as an adequate dose. It is well established that even with larger doses a negative response is no proof of complete vagotomy.]

H. Daintree Johnson

2663. **Diagnosis of Volvulus of the Stomach.** (Ein Beitrag zur Diagnostik des Magenvolvulus)

W. S. REICHEL. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **71**, 900–905, Oct., 1949. 5 figs., 11 refs.

Five cases are described of gastric torsion about the mesenteric or horizontal axis. The common type of torsion, which takes place about the longitudinal axis, is nearly always due to pressure from outside, and rarely causes the symptoms which lead to its discovery. Mesenteric volvulus, on the other hand, arises as an exaggeration of the cascade stomach in which the position may at any time become worse and lead to an acute surgical emergency. The possibility of volvulus should be thought of when a cascade stomach is associated with weakness or paralysis of the left diaphragm. The upper pouch becomes overdistended and sinks down posteriorly. To fill in the space the greater curve and antrum ascend anteriorly so that the pylorus comes to lie in front of the cardia and the first part of the duodenum passes vertically downwards. A less common type arises from the reverse cascade stomach where the upper pouch lies anteriorly in front of a gas-distended transverse colon. The combination of an overfilled upper pouch, a weak left diaphragm, and violent sudden changes in intra-abdominal pressure such as those produced by sneezing and coughing may lead to prolapse of the stomach forwards over the transverse colon and ascent of the pylorus behind the cardia.

Postural exercises are advised to empty the upper pouch of a cascade stomach associated with a weak left diaphragm, especially if the patient is confined to bed with an upper respiratory infection.

[These cases are not uncommon and the diagnosis is apt to be missed by specialists in cardiac and pulmonary disease. Much can be done to help these patients.]

Denys Jennings

2664. **The Configuration and Relations of the Stomach During Gastroscopy**

E. D. PALMER and E. L. REA. *Gastroenterology* [*Gastroenterology*] **14**, 131–146, Jan., 1950. 13 figs., 12 refs.

2665. **The Influence of Naturally Carbonated Mineral Water on Gastric Motility and the Secretion of Hydrochloric Acid**
F. A. HELLEBRANDT and S. J. HOUTZ. *Archives of Physical Medicine* [*Arch. phys. Med.*] **31**, 25–34, Jan., 1950. 5 figs., 35 refs.

See also Section Radiology, Abstracts 2485-6.

LIVER

2666. **Activated Diuresis in Jaundice.** (La diurèse activée au cours des ictères)
J. GRENIER. *Presse Médicale* [*Pr. méd.*] **57**, 1022–1024, Nov. 2, 1949. 6 figs., 6 refs.

The author observed that in cases of acute and chronic icterus fresh blood transfusions were harmless and had a beneficial therapeutic effect by improving the general condition. He also found that a diuresis followed the transfusion in some cases, but not in others, and applied this distinction as a diagnostic test in a number of cases. Before the test the urinary output was observed over a period of 3 days, and then 6 or more transfusions, each of 100 to 120 g. of fresh blood, were given at 2-day intervals.

A rapid or progressive diuresis of from 1 to 3 litres daily occurring within a week was regarded as a positive result, indicating a permeable biliary tract. This group included cases of infective, toxic, cirrhotic, and suppurative cholangitic jaundice. When no diuresis occurred the test was negative, and was considered to indicate practically complete obstruction of the biliary tract. Irregularities in the diuresis were sometimes associated with pyrexia due to exacerbations of suppurative cholangitis or hepatitis. The cause of the diuresis is so far unknown, but the author suggests that the transfusion may alter the humoral lipoprotein levels or may have some direct effect upon the liver itself. A search is being made for other substances which might have the same general effects as fresh blood.

I. Ansell

2667. **Metabolic Study of Gynecomastia Associated with Liver Disease**
E. L. COODLEY and W. E. MOLLE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **218**, 531–539, Nov., 1949. 2 figs., 30 refs.

The authors review the relation between gynaecomastia, cirrhosis of the liver, and endocrine disturbances, illustrating their subject with a description of a single case. Their patient, a 30-year-old Mexican male, complained of respiratory and gastro-intestinal symptoms and had a history of long-standing dietary deficiency aggravated by alcoholism. The notable features were signs of pneumonia, jaundice, liver enlargement, diminution of the axillary, chest, and pubic hair, diffuse hypertrophy of the left breast (with no abnormality of the nipple), an atrophic left testicle, and many spider angiomata.

After treatment of the pneumonia, the patient was given daily injections of oestrone for 2 weeks, the dose being 40,000 units daily for the first week and 120,000 units daily for the second. This resulted in a slight increase in the size of the left breast, improvement in liver function as shown by routine tests (including biopsy), and a decrease in the number of angiomata, implying remarkably rapid liver recovery on a normal hospital diet. Change to a high-protein, high-carbohydrate, low-fat diet with protein, vitamin, and liver-extract supplements led to further clinical improvement, with a decrease in the size of the left breast and in the number of angiomata. A fall in oestrogen excretion accompanied this clinical improvement, while an increase in libido, in the size of the right testicle (that of the left remaining unaltered) and in the urinary ketosteroids suggested a close correlation between liver and adrenal function and gonadal activity. The unilateral gynaecomastia is explained by assuming a different degree of sensitivity to circulating oestrogens in the two breasts. The period of follow-up is not stated. In their discussion the authors review the causes of gynaecomastia and include malnutrition and vitamin-deficiency disease. [Their report is interesting for its study of, and emphasis on, liver function in this condition.]

R. N. Johnston

2668. **Needle Biopsy of the Liver in Alcoholic Patients**
S. SANES, R. C. BAHN, W. H. C. CHAPPLE, and N. CHASSIN. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **49**, 2677–2681, 1949. 14 refs.

Needle biopsy of the liver was performed on 80 chronic alcoholic patients, mostly admitted in an acute state of intoxication to the alcoholic or psychiatric wards of the Meyer Memorial Hospital in Buffalo, New York. There was some selection of cases in which evidence suggestive of liver disease was present. The Vim–Silverman technique was used and no serious complication occurred. The biopsy specimens showed fatty changes in 36, fatty changes with cirrhosis in 7, portal cirrhosis in 20, normal appearances in 13, and unclassified findings in 4 cases. These findings were usually at variance with the clinical assessment. Hepatic function tests (12 on each patient) gave abnormal results in 20% of the cases of fatty liver and in 50% of the cases of cirrhosis. Iron-containing pigments were demonstrated in 20 cases. The authors suggest that needle biopsy of the liver is the only satisfactory method of detecting hepatic disorders in the alcoholic patient.

R. B. Terry

2669. **Malnutrition as a Cause of Hepatic Cirrhosis.** (Hunger als Ursache der Leberzirrhose. Die Zirrhose der Heimkehrer)
H. KALK. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **75**, 225–229, Feb. 17, 1950. 2 figs., 15 refs.

Of 13 prisoners of war returning home to Germany in 1949 with enlargement of the liver and spleen, evidence of cirrhosis of the liver was obtained by means of peritoneoscopy and liver puncture in 5 cases. The condition is attributed to starvation, which leads first to fatty liver and then to cirrhosis. These 5 patients had histories of dysentery, malaria, typhus, or gall-bladder disease,

but all of them had been underfed and had suffered from famine oedema during captivity. In 3 of the cases of cirrhosis, haemochromatosis was also present.

H. E. Magee

2670. **On Hepatitis.** (Adatok a hepatitis-kérdéshez) B. KELLNER. *Orvosi Hetilap* [*Orv. Hetil.*] **90**, 481–488, Aug. 21, 1949. 3 figs., bibliography.

In the course of 1,500 post-mortem examinations, the author encountered 20 cases of death from infective hepatitis; in none of these cases was the source of infection known. In 6 acute cases all the changes of acute yellow atrophy were present, with much destruction of liver cells; in 3 subacute and 6 chronic cases there was regeneration of liver cells, but where there had been an acute terminal phase there was marked destruction of the regenerated cells. In 5 children the histological picture was the same as in adults, although clinically the hepatitis had been less marked and two of them had had no icterus. *Dushanka Wolstenholme*

2671. **Electrophoretic Studies of the Serum Proteins in Biliary Cirrhosis**
K. STERLING and W. E. RICKETTS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 1469–1476, Nov., 1949. 3 figs., 20 refs.

In a series of 10 cases of obstructive biliary cirrhosis the serum albumin and globulin levels were determined, hepatic function assessed by a number of tests, and electrophoretic analysis of the serum proteins carried out. This last showed there to be a lowered serum albumin fraction and a raised β-globulin level in all cases, and in 8 cases a raised γ-globulin level. The degree of abnormality of the electrophoretic analysis appeared related to the severity of the condition; thus in 2 cases in which the disease appeared quiescent and the serum bilirubin concentration was normal, only slight changes were found in the serum protein fractions, while in 5 cases in which active ascending cholangitis was present and the serum bilirubin value was raised, the serum albumin level was below 3 g. per 100 ml. and the β- and γ-globulin fractions were increased to a varying extent. The serum of 3 patients with a prolonged history of obstructive jaundice and with secondary xanthomatosis showed marked abnormality, the β-globulin fraction being very much increased. This increase was reduced by cold ether extraction of the serum and was thought to be due in part to an increased lipoprotein content of the serum. A return of the electrophoretic pattern towards normality was observed in one case when biliary obstruction was relieved. *F. W. Chattaway*

2672. **Electrophoretic Studies of the Serum Proteins in Virus Hepatitis**
W. E. RICKETTS and K. STERLING. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 1477–1486, Nov., 1949. 5 figs., 25 refs.

The electrophoretic pattern of the serum proteins was studied in 21 clinically typical cases of hepatitis, 19 of which were of infective hepatitis and 2 of homologous serum hepatitis, liver function tests being carried out at the same time. Of 10 cases in the acute phase, the albumin value was diminished in all, the β-globulin level was raised in 7, and the γ-globulin level raised in 7. The serum of patients with severe acute hepatitis tended to show a greater degree of abnormality than that in the mild cases, but there was no strict correlation between the electrophoretic pattern and the clinical condition. Serial electrophoretic analyses in 5 cases showed a return of the serum proteins to normal in 2 cases, but persistent abnormalities were found in the other 3, although clinically they had recovered. Late follow-up studies (10 to 36 months after recovery) in 11 cases of acute virus hepatitis showed residual abnormalities in both albumin and globulin fractions in 8 cases. *F. W. Chattaway*

2673. **Studies in Methionine Metabolism. II. Fasting Plasma Methionine Levels in Normal and Hepatopathic Individuals in Response to Daily Methionine Ingestion**
L. W. KINSELL, H. A. HARPER, G. K. GIESE, S. MARGEN, D. P. MCCALLIE, and J. R. HESS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 1439–1450, Nov., 1949. 6 figs., 3 refs.

The level in the plasma of fasting subjects and the urinary excretion of D- and L-methionine following their administration by mouth were studied, the dosage being 9 mg. DL-methionine per day for 2 weeks and this period being preceded and followed by one-week control periods; where toxic symptoms appeared methionine administration was continued for only 2 days and control periods were correspondingly shortened. Normal subjects showed a fasting level for L-methionine of 0·25 to 0·48 mg. per 100 ml., which rose to levels not exceeding 2 mg. per 100 ml. on methionine administration and returned to normal levels in 24 to 48 hours after cessation of the methionine dosage. D-Methionine was not present in the resting plasma but appeared in amounts up to 2·4 mg. per 100 ml. with an equally rapid return to normal. Patients with acute hepatitis showed a retention of methionine during administration (plasma levels of L-methionine up to 18 mg. per 100 ml., with smaller rises in D-methionine level), the degree of retention varying with the state of liver function as determined by several tests, and returning to normal rapidly after cessation of dosage. Three cases of chronic viral hepatitis showed a similar picture with very high levels of L-methionine (40 mg. per 100 ml.) and a raised urinary level in a severe case. Several other patients with liver dysfunction retained a large amount of L-methionine, the quantity varying with the degree of liver damage; the only exception was in one case of haemochromatosis where the L-methionine plasma levels were normal.

F. W. Chattaway

2674. **Hepatitis and its Sequelae, Including the Development of Portal Cirrhosis. Observations on One Hundred Cases**
M. F. KOSZALKA, M. C. F. LINDERT, H. M. SNODGRASS, and H. B. LERNER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **84**, 782–797, Nov., 1949. Bibliography.

See also Section Pathology, Abstract 2503.

Endocrine Disorders

THYROID

2675. **The Effects of Iodides and Other Halides Given with Thiouracil**
J. K. W. Ferguson and E. A. Sellers. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 177–181, Oct., 1949. 9 refs.

Rats were supplied with drinking water containing 0·1% of thiouracil and, in some cases, 0·02 to 0·5% of iodide. After 2 to 6 weeks the thyroids of rats receiving the iodide were 20 to 30% lighter than those of the others. The metabolic rate was the same in both groups. Histologically, the thyroid follicles of the rats receiving iodide contained more colloid and showed less hyperplasia than those of the others. *V. J. Woolley*

2676. **A Comparison of the Anti-thyroid Activity of *para*-Aminobenzoic Acid and Thiouracil Compounds**
J. F. Goodwin, H. Miller, and E. J. Wayne. *Lancet* [*Lancet*] **2**, 1211–1214, Dec. 31, 1949. 2 figs., 14 refs.

para-Aminobenzoic acid (PAB) has been used clinically for various therapeutic purposes, particularly in leukaemia. It has been given in doses of up to 4 g. 2-hourly and has produced leucopenia, a tendency to haemorrhages, and renal glycosuria. Several deaths have been reported from overdosage. It has also been given in much smaller doses for thyrotoxicosis. The authors treated 9 patients with thyrotoxicosis with 4 g. of PAB daily and one with 8 g. daily; there was no effect in 6 cases, slight improvement in 3, and full control in one. No toxic effects were observed. Subsequent thiouracil treatment [dose not recorded] in 8 of the 10 patients resulted in no change in 2 cases, slight improvement in 2, great improvement in one, and complete control in 3, from which it is concluded that thiouracil is the more effective drug.

Finally, the authors examined the effect of doses of 4 to 6 g. of PAB on the rate of uptake of radioactive iodine by the thyroid gland in 17 normal subjects and compared it with the effect of 200 to 300 mg. of methylthiouracil. They found that 200 mg. of methylthiouracil was more effective in this respect than 4 g. of PAB, and that for the successful treatment of thyrotoxicosis it would be necessary to use a toxic dose (6 g. or more) of the latter drug. *A. C. Crooke*

2677. **The Effect of Methyl- and Propyl-thiouracil on the Function of the Ovary.** (Methyl- és propylthiouracil hatása a petefészek-működésre)
F. Szontágh and G. Lichner. *Orvosi Hetilap* [*Orv. Hetil.*] **90**, 683–685, Nov. 13, 1949. 2 figs., 34 refs.

The authors gave methylthiouracil (0·1 g. per kg. body weight) or propylthiouracil (0·05 g. per kg.) in 10% solution in water by stomach tube daily to mature female rats, the regularity and duration of whose oestrus had been observed. Over a period of treatment of 2 months it was found with both drugs that oestrus was very greatly reduced in all animals. Examination of the ovaries revealed few or no follicles and much luteinization. *Dushanka Wolstenholme*

2678. **Exophthalmic Goiter in Children: Treatment with Propylthiouracil**
A. S. Jackson and H. B. Haley. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **218**, 493–499, Nov., 1949. 3 figs.

This article is based on experiences gained in the management of 26 cases of thyrotoxicosis in children up to the age of 16 years, 8 of whom had been given thiouracil or propylthiouracil. It is pointed out that too much stress should not be laid upon estimation of basal metabolic rate in view of the undue susceptibility of these children to upper respiratory infections. A blood pressure of 140/50 mm. Hg is a typical finding. Sometimes treatment by rest, sedatives, and extra feeding is sufficient. Indication for operation is based on experience that operation is the best type of treatment in the particular case, on failure of medical therapy (including complications such as leucopenia), and on persistence of an enlarged, although no longer toxic, thyroid. Propylthiouracil, in particular, causes a marked increase in the vascularity of the thyroid and thereby renders the operation technically more difficult. Considerable time and effort are spent before operation in gaining the confidence of the child. The operation consists of a subcapsular subtotal excision of the hyperplastic thyroid tissue (preferably by the electro-surgical knife), superficial cervical nerve block analgesia with 1·5% procaine, but without adrenaline, being used. Children over the age of 12 years are given adequate pre-operative sedation by means of " pantopon ", scopolamine, and " nembutal ", the dosage depending upon the weight of the child. Post-operative care is facilitated by the fact that the conscious, co-operative patient can take Lugol's iodine orally immediately after the operation.

The authors consider that there is no single rule for predicting the outcome of the various forms of treatment employed. Whereas propylthiouracil is less toxic than thiouracil, it does not usually do away with the need for surgery, which is rendered more difficult by the greatly increased vascularity which the drug produces. *I. H. Milner*

2679. **Seasonal Variations in Thyrotoxicosis**
M. E. Morgans and W. R. Trotter. *Lancet* [*Lancet*] **2**, 1083–1084, Dec. 10, 1949. 1 fig., 10 refs.

Observations on 122 patients with thyrotoxicosis treated with methylthiouracil between June, 1945, and June, 1949, showed that in 59 of the cases the dosage could be gradually reduced and the drug finally stopped,

the patient making an uninterrupted recovery. In the other 63 patients, however, signs of thyrotoxicosis became accentuated at one time or another, necessitating a temporary increase in the dose of this drug. This happened far more frequently in the first 5 months of the year than in the last 7 months. Further analysis of those cases in which the patients was able to dispense with treatment showed that 60% of these were able to stop treatment in the 4 months October to January. It thus appears that there is a definite seasonal influence in thyrotoxicosis, an increase in the length of daylight being associated with an increased number of exacerbations. The mechanism of this is discussed and it is suggested that it may be due to stimulation of the pituitary by increasing length of daylight (this is known to affect the output of gonadotrophic hormone in some mammals and birds) or alternatively to seasonal variation in the amount of goitrogenic substances in the diet (as is known to occur in the case of cabbage). *C. Bruce Perry*

2680. **Oral Thyroxine in Treatment of Myxoedema**
F. D. HART and N. F. MACLAGAN. *British Medical Journal* [*Brit. med. J.*] **1**, 512–518, March 4, 1950. 8 figs., 11 refs.

Over a period of 18 months 9 cases of myxoedema have been treated at the Westminster Hospital by the oral administration of various synthetic thyroxine derivatives. Each of the preparations used (L- and DL-thyroxine, L- and DL-thyroxine sodium, and DL-N-formyl thyroxine) produced satisfactory clinical results when given in appropriate dosage. The most active preparation was L-thyroxine sodium (average daily dose, 0·15 to 0·3 mg.). This preparation is now available commercially at a price which compares favourably with that of thyroid extract, and being a pure substance possesses the advantage that it does not require biological or chemical standardization. As with thyroid extract overdosage is a real danger. Therefore the dosage used should be the smallest which will relieve symptoms.

In 3 patients in whom the condition was stabilized on a maintenance dose, estimations of the basal metabolic rate at various intervals after the last dose of thyroxine showed little significant variation over a period of 24 hours. This suggests that a single daily dose of thyroxine is probably sufficient. *G. Ansell*

2681. **Hyperthyroidism in Patients Over Sixty**
E. C. BARTELS and J. W. KINGSLEY. *Geriatrics* [*Geriatrics*] **4**, 333–340, Nov.–Dec., 1949. 2 figs.

Of the first thousand patients treated pre-operatively with antithyroid drugs at the Lahey Clinic, Boston, 124 (12%) were over 60 years of age. The present paper is concerned with this group of elderly thyrotoxic patients.

Primary hyperthyroidism (P.H.) occurred less frequently than hyperthyroidism secondary to adenomatous goitre (S.H.); the reverse is the case in younger age groups. As in the young, approximately 80% of both groups were females. The commonest presenting symptom in P.H. was loss of weight, in S.H. general muscular weakness. The duration of symptoms was under 3 years in P.H. and usually over 3 years in S.H., but in both it was longer than in younger groups. Weight loss was considerable in both P.H. and S.H., but was less commonly a complaint in S.H. because of its more gradual occurrence. Cardiac symptoms (dyspnoea and palpitations), although common in S.H., were less common than in S.H. in younger patients. Nervousness, increase in appetite, and gastro-intestinal symptoms were infrequent. Tremor and intolerance of warmth were frequently encountered in P.H., but less commonly than in younger patients.

The commonest physical sign in both P.H. and S.H. was increased body warmth. Eye signs were uncommon in P.H. and not seen in S.H. Tachycardia was not a notable feature; the pulse rate in one-third of cases of both P.H. and S.H. was less than 100 per minute.

Auricular fibrillation and congestive heart failure, both singly and together, were common in both groups but more so in S.H. than P.H. The basal metabolic rate was invariably raised above +10% and was generally higher in P.H. than in S.H. Diabetes mellitus was also present in 16% of the cases of S.H. but in only 4% of those of P.H.

Cases of S.H. responded more slowly to antithyroid drugs than did those of P.H. The over-all clinical picture was considered a more reliable guide to dosage than the basal metabolic rate. Drug reactions were less common with propylthiouracil than with other compounds. Lugol's iodine was given to all patients for 3 weeks immediately before operation. Subtotal thyroidectomy was performed in 123 cases with a mortality of 0·8% (1 death), which represents a considerable improvement on the 2·5% mortality in a comparable group of patients before 1943. It is considered that antithyroid drugs have reduced the post-operative morbidity and period of hospital stay by 75%. Cancer of the thyroid was not found in any of the resected glands.

All patients were followed up for from 3 months to 5 years. Thyrotoxic symptoms have not recurred or persisted in any patient. Myxoedema developed in 7 cases, and persistent hypoparathyroidism in one.
P. D. Bedford

PITUITARY AND SUPRARENALS

2682. **Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy**
J. R. ELKINGTON, A. D. HUNT, L. GODFREY, W. W. MCCRORY, A. G. ROGERSON, and J. STOKES. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 1273–1279, Dec. 31, 1949. 7 figs., 24 refs.

Adrenal cortical extracts and pituitary adrenocorticotrophic hormone (ACTH) have been found to be effective in the treatment of conditions other than rheumatoid arthritis, such as rheumatic fever, lupus erythematosus, and gout. This response would seem to indicate some relationship between these various diseases (as has previously been suggested by Arnold Rich). This paper deals with the treatment with ACTH of 2 cases of rheumatoid arthritis, 2 of disseminated lupus erythe-

matosus, 1 of dermatomyositis, 2 of rheumatic fever, and 1 of status asthmaticus. The purpose of the investigation was to study the clinical course, toxic complications, and the degree of stimulation and response of the suprarenal gland. These changes were assessed by means of eosinophil and total leucocyte counts, estimations of the sodium, potassium, chloride, and nitrogen balance, and the output of urinary 17-ketosteroids. Two patients, one with arthritis and one with lupus erythematosus, relapsed completely, despite prolonged treatment and increased dosage, while 2 others, one with lupus erythematosus and one with dermatomyositis, remained in remission. In one case of arthritis and in the case of asthma the response to the drug was dramatic. In 5 cases there was an eosinophilic leucopenia following treatment, and in all cases the sodium content of the urine was reduced. Consistent changes in the serum sodium and chloride levels were not found. The effects on the serum potassium content and the nitrogen balance were equivocal. It would appear that administration of ACTH decreases carbohydrate tolerance, as 13 patients developed a slight glycosuria. The excretion of 17-ketosteroids was increased in all cases. Severe potassium deficiency and also encephalopathy, either drug-induced or due to the disease, occurred in the case of acute dermatomyositis. One patient with acute rheumatoid arthritis developed signs of Cushing's syndrome after prolonged treatment; there was, however, neither hypertension nor diabetes. One case failed to respond and the patient died, the presence of antihormones being a possible explanation.

It is concluded that adrenocorticotrophic hormone obviously exerts a profound influence on collagen disease. Presumably it acts by " supporting " the adrenal, which is adversely affected in these hypersensitive states. The technique of repeated short courses of treatment may help to prevent toxic manifestations. The authors sound a wise warning against administration of the drug without laboratory control. *Paul B. Woolley*

2683. **Studies on the Effect of the Administration of Pituitary Adrenocorticotrophic Hormone (ACTH) to a Case of Loeffler's Syndrome and a Case of Tropical Eosinophilia**

P. HERBERT, J. A. DE VRIES, and B. ROSE. *Journal of Allergy* [*J. Allergy*] **21**, 12–24, Jan., 1950. 5 figs., 14 refs.

A patient suffering from Loeffler's syndrome received four intramuscular injections of 50 mg. of pituitary adrenocorticotrophic hormone (ACTH) at half-hourly intervals. During this time the total leucocyte count increased from about 7,000 to 13,000 per c.mm. and then fell to 11,000 per c.mm., while the number of eosinophils fell steadily from 2,865 to 54 per c.mm. During the next week the eosinophil count rose again to a figure between 1,100 and 1,500 per c.mm., while the total leucocyte count returned to its previous level of 7,000 per c.mm. Radiographs of the chest showed some increase of the density of the infiltrations 4 hours after the first injection of ACTH, but one week later there was a definite diminution in the infiltration. The blood histamine content was not changed. In a patient with tropical eosinophilia who received two injections of 120 mg. of ACTH separated by an interval of 5 hours there was a similar transient increase in the leucocyte count; the eosinophil count increased initially from 39,000 to 49,000 per c.mm., and then fell to 25,700 per c.mm. *H. Herxheimer*

2684. **Pituitary Adrenocorticotropic Hormone (A.C.T.H.) as a Tool of Clinical and Laboratory Research**

T. D. SPIES and R. E. STONE. *Lancet* [*Lancet*] **1**, 11–14, Jan. 7, 1950. 3 figs., 7 refs.

In this paper the authors describe the effects of intramuscular injections of pituitary adrenocorticotrophic hormone (ACTH) in 4 patients suffering from different diseases.

ACTH was given in 15-mg. doses 4-hourly to a man with rheumatoid arthritis. The usual objective and subjective improvement began within 24 hours of the initial injection. During the 4 days of treatment the blood pressure rose slightly and he gained 11½ lb. (5 kg.) in weight, due to water retention as evidenced by the development of pitting oedema at the ankles. Oedema disappeared and the weight returned to its previous level within a week of stopping treatment. There was no improvement in the marked anaemia (erythrocytes 2,200,000 per c.mm.; haemoglobin 7·1 g. per 100 ml.). Symptoms began to return 12 days after stopping treatment, and relapse to the condition before treatment was complete within 8 weeks. The patient was then given intramuscular injections of 7 different steroids, each for 4 days at a daily dose of 200 or 300 mg. (except in the case of deoxycortone acetate, for which the total dose was 20 mg.). The substances administered were: pregnene-(4)-triol-(17α,20β,21)-one-(3)-diacetate; pregnane-3, 12, 20-trione; 17-methyl Δ 5-androstendiol-3 (β), 17 (α); 17-α-hydroxyprogesterone; 17-α-hydroxy-11-desoxycorticosterone-21-acetate; deoxycortone (desoxycorticosterone) acetate; ergostanyl acetate. No significant effects were observed with any of these substances. The patient now received a further course of ACTH and again showed the characteristic improvement and rapid relapse on cessation of treatment. It is reported that the above findings were typical of those observed in 4 other patients with rheumatoid arthritis similarly treated.

A single 30-mg. dose of ACTH produced symptomatic improvement within 30 minutes in a patient with atypical mild gout (blood uric-acid level 6·7 mg. per 100 ml. or more). Within 12 hours relief was complete and at the time of reporting, 4 months later, there had been no recurrence. The only significant laboratory finding was a profound and sustained fall in blood uric-acid level: 4·2 mg. per 100 ml. after 2 days; 1·7 mg. per 100 ml. after 4 days; and 3·9 mg. per 100 ml. after 2 months. In 3 other patients relief from symptoms of acute gout is stated to have been obtained when ACTH injections were started early enough.

The third case was one of psoriasis with arthritic manifestations; this woman received 18 doses each of 15 mg. of ACTH at 6-hourly intervals. Within 70 hours of the start of treatment some amelioration in the skin

lesions was noted; 24 hours later slight improvement in the joint condition began. The patient experienced marked elation. A week after she stopped treatment the skin condition began to deteriorate and a week later the arthritic symptoms began to return.

The fourth case was that of a woman complaining of attacks of asthma, hay-fever, urticaria, and pain in the wrists, hands, knees, and ankles. She had eosinophilia (1,000 to 3,000 eosinophils per c.mm. blood) and produced thick sputum containing many eosinophils. She received 10 mg. of ACTH twice daily for 4 days. Within 2 days of starting treatment all symptoms had disappeared, the eosinophil count having fallen to normal within a few hours of the first injection. Ten days after stopping treatment the joint symptoms began to return. The eosinophilia returned 3 days after the last injection.

[The title of this paper is quite misleading.]

G. I. M. Swyer

2685. **The Effect of Cortisone on the Production of Granulation Tissue in the Rabbit.** (L'effet du cortisone sur la production du tissu de granulation chez le lapin)
C. RAGAN, E. L. HOWES, C. M. PLOTZ, and J. W. BLUNT. *Comptes Rendus des Séances de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **230**, 327–329, Jan. 16, 1950. 2 figs.

In wounds produced experimentally in rabbits treated with cortisone there is a striking reduction in the formation of new connective tissue: new blood vessels were few or entirely absent. After 8 days' treatment there were compact nests of fibroblasts surrounding the previously existing blood vessels. *G. M. Findlay*

2686. **The Treatment of Addison's Disease by the Intraoral Administration of Desoxycorticosterone Acetate Tablets**
E. ANDERSON, L. W. KINSELL, T. C. DANIELS, and E. HENDERSON. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **9**, 1324–1332, Dec., 1949. 21 refs.

In 14 cases of Addison's disease the patient has been successfully maintained sufficiently well to follow light employment for 18 months to 2 years by the intraoral use of tablets of deoxycortone acetate without any supplementary salt. The tablets consist of 2 mg. of the hormone contained in 200 mg. of polyethylene glycol wax and the average maintenance dose is 4·5 mg. of hormone daily; the dose had to be raised during periods of active pulmonary tuberculosis in 2 patients. The dose is given by placing a tablet under the tongue one to four times a day and allowing it to dissolve there.

Peter C. Williams

2687. **The Syndrome of Hypopituitarism**
H. L. SHEEHAN and V. K. SUMMERS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **18**, 319–378, Oct., 1949. 18 figs., bibliography.

This analysis of the syndrome of hypopituitarism is based solely on those cases in which the condition of the pituitary after death warrants the description of the lesion as chronic and severe and not interfering with surrounding structures. A search of the literature and of the authors' own files revealed only 97 of such cases in which the pituitary contained chronic fibroid lesions, large cysts, or tumours, or had been removed by operation.

The patients mostly live for 5 to 15 years under these conditions, but may survive for 40 years. The chief clinical symptoms are atrophy of the thyroid, adrenals, gonads, and genital tract. Loss of body weight is not, as is usually supposed, a cardinal symptom of the disease. Analysis of the recorded findings in the 97 acceptable cases showed that their state of nutrition at death, and more particularly 6 months beforehand, was certainly better than in 500 people dying of other complaints. In patients classified as having slight lesions or otherwise excluded from the list of 97, emaciation did occur more frequently. This suggests that the diagnoses in these cases were in fact incorrect because of the presence of emaciation or that wasting is a symptom of hypothalamic pressure. Progeria is another commonly accepted symptom of hypopituitarism for which the authors find no evidence.

Associated and probably secondary symptoms are: loss of weight of viscera (liver, kidneys, heart, and pancreas) unrelated to changes in body weight; loss of sex function and libido; loss of pubic and axillary hair; dryness of skin with loss of pigment (the failure to tan in artificial sunlight is a distinctive symptom); and low basal metabolism with myxoedematous facies. Anaemia (usually normochromic but occasionally macrocytic and unresponsive to administration of liver) and gastric achylia are common. The patients are sensitive to insulin in a tolerance test and unresponsive to the resultant hypoglycaemia. There is a failure of water diuresis, and a Kepler test gives results like those in Addison's disease. Death generally occurs in coma, usually precipitated by vomiting and anorexia or by intercurrent illness. The differential diagnosis is summarized.

Reports of 5 severe, 3 moderate, and 2 minor cases of hypopituitarism with necropsy reports and of 9 surviving cases of post-partum necrosis of the pituitary are given in an appendix. [This is a full and careful review.]

Peter C. Williams

2688. **Anemia and Arthritis in a Case of Pituitary Insufficiency Confirmed at Autopsy.** [In English]
H. HORTLING. *Acta Endocrinologica* [*Acta endocrinol., Kbh.*] **3**, 181–200, 1949. 5 figs., 46 refs.

The case is reported of a man aged 54 years with symptoms of Simmonds's disease which had progressed for 19 years. He died of cachexia and was found to have extensive fibrosis of the pituitary gland. Two years before death he fell and injured his right knee, in which arthritis and ankylosis subsequently developed. The relation of arthritis to Simmonds's disease is discussed.

A. C. Crooke

2689. **The Pathology and Physiology of Diabetes Insipidus: The Polydipsic Form.** (Étude physiopathologique du diabète insipide: la forme polydipsique)
R. KOURILSKY and E. FOURNIER. *Annales de Médecine* [*Ann. Méd.*] **50**, 529–574, 1949. 14 figs., 24 refs.

Dermatology

2690. **Polyneuritis as an Apparent Complication of Calciferol Treatment and Some Observations on Its Local Use**
G. H. V. CLARKE. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **61**, 409–413, Dec., 1949. 1 fig., 10 refs.

Attention is drawn to the scanty literature on the use of calciferol locally in the treatment of lupus vulgaris, and a case is reported in which ulcerative lupus of thigh and face appeared to respond to this measure. The patient was a farmer, aged 64 years, whose lupus was of long duration and in whom the administration of calciferol internally was followed by pyrexia and toxic symptoms, with acute polyneuritis. He recovered from the latter affection after liver and aneurin (thiamine) had been administered. *John T. Ingram*

2691. **The Mechanism of Action of Vitamin-D Therapy in Skin Tuberculosis.** (Über den Wirkungsmechanismus der Vitamin-D-Therapie bei Hauttuberkulose)
R. BRETT and K. H. ECKES. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **74**, 859–863, July 15, 1949. 4 figs., 16 refs.

The effects of a salt-free diet and of vitamin D in the treatment of skin tuberculosis are compared. Both are effective against lupus vulgaris, though useless or dangerous against tuberculosis of the lungs. The administration of large doses of vitamin D was found to produce an increased urinary excretion of sodium chloride, a reduction in serum chloride level, and a marked increase in the calcium content of affected skin—without histological evidence of calcification. The authors suggest that the mode of action of vitamin D in lupus is to be found in the changes it induces in the mineral-salt content of the skin. In view of the dangers of giving very high dosage of the vitamin, they suggest that lower doses given in combination with a salt-free diet would be equally effective.
Dushanka Wolstenholme

2692. **Congenital Ichthyosiform Erythroderma.** (Ipercheratosi ittiosiforme rubra)
A. TOSTI. *Annali Italiani di Dermatologia e Sifilografia* [*Ann. ital. Derm. Sif.*] **4**, 509–514, Nov.–Dec., 1949. 5 figs., 10 refs.

2693. **Dermatitis Following the Use of Pyribenzamine and Antistine**
W. B. SHERMAN and R. A. COOKE. *Journal of Allergy* [*J. Allergy*] **21**, 63–67, Jan., 1950. 6 refs.

In 3 patients with a history of allergic disease, administration of antihistaminic drugs caused an exacerbation of contact dermatitis. In 2 cases this was due to "pyribenzamine" ointment and in one to "antistin" eye drops, and the exacerbation occurred after the drug had been used for several days. The first patient gave a positive patch-test reaction to pyribenzamine only, the second also to "neoantergan" and "thenylene", the third to all the above drugs and also to antistin, "diatrine", "neohetramine", "trimeton", and "benadryl", but not to "thephorin". *H. Herxheimer*

2694. **Eosinophilic Granulomas of the Skin**
E. A. OLIVER, J. R. WEBSTER, J. E. GINSBERG, and H. S. STEINBERG. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **60**, 701–716, Nov., 1949. 6 figs., 9 refs.

The salient features of the type of granuloma of the skin in which, on histological examination, a striking number of eosinophil cells are found are reviewed and its possible relation to other general, local, and allergic diseases discussed. Two cases are reported with details of pathological investigations and treatment. One patient was apparently cured by treatment with *x* rays directed towards the main concentrations of the reticuloendothelial system.

The authors present these cases with the plea that others publish their investigations. They suggest that only by pooling all the available information can rapid progress be made in the study of this group of diseases.
G. B. Mitchell-Heggs

2695. **Multiple Hemorrhagic Sarcoma and Diabetes Mellitus. Review of a Series, with Report of Two Cases**
W. B. HURLBUT and C. S. LINCOLN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **84**, 738–750, Nov., 1949. 5 figs., 18 refs.

The literature concerning multiple idiopathic haemorrhagic sarcoma (Kaposi's disease) is reviewed and the clinical course, histopathology, and pathogenesis of this rare disease are discussed. The occasional association with leukaemia and other reticuloses is noted. In the series of 13 cases studied by the author, 6 of the patients suffered from diabetes mellitus, and in one male patient the presence of gynaecomastia and hot flushes suggested endocrine imbalance. The clinical course in 2 cases and the necropsy findings in one of them are described in detail. Attention is drawn to the fact that oedema of one or both legs may be an early symptom.
John T. Ingram

2696. **Vitamin A and Choline in Ichthyosis.** (Axeroftolo e colina negli ittiosici)
P. CACCIALANZA and R. VACCARI. *Acta Vitaminologica* [*Acta vitamin., Milano*] **6**, 247–250, Dec., 1949. 2 figs., 17 refs.

A daily dose of 0·5 to 1 g. of choline, given by mouth, raised the blood vitamin-A level in ichthyotic patients as well as in normal subjects. Vitamin A and choline given simultaneously raised the blood vitamin-A level in ichthyotics much higher than did the administration of the same dose of vitamin A alone. *Z. A. Leitner*

Venereal Diseases

SYPHILIS

2697. **Neurosyphilis—III. Evaluation after Three Years of Treatment with Penicillin Alone and with a Combination of Penicillin and Malaria**
A. C. CURTIS, W. T. KRUSE, and D. H. NORTON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 527–536, Nov., 1949. 8 figs., 8 refs.

The results 1 to 3 years after treatment with penicillin and malaria in 380 cases of neurosyphilis are here reported. All patients received a total dosage of 4 mega units of penicillin in water, and about one-half of the series also received malarial therapy (50 hours or more of fever above 103·5° F. (39·7° C.)). The results of clinical and cerebrospinal-fluid examination are set out in statistical and tabular form. The response in various types of neurosyphilis, including tabes and paresis, was equally good to penicillin alone and to the combined therapy. *V. E. Lloyd*

2698. **The Effects of Crystalline Penicillin G and of Impure Penicillin on Experimental Syphilis.** (Effets de la pénicilline G cristallisée et des pénicillines impures dans le traitement de la syphilis expérimentale)
C. LEVADITI, A. VAISMAN, and G. HAGEMANN. *Presse Médicale* [*Pr. méd.*] **57**, 1249–1250, Dec. 31, 1949. 7 refs.

The antisyphilitic efficacy of crystalline penicillin G and of two impure penicillin preparations was compared in rabbits with scrotal syphilomata and in infected mice. Adequate doses of penicillin were given by subcutaneous injection and the effect on the rabbits assessed in respect of time of disappearance of treponemes from scrotal lesions, speed of healing, and sterilization of the lymphatic system as demonstrated by lymph-node transfer to other rabbits. The mice, infected for 305 days, were killed after 22 to 25 days' treatment and the presence or absence of treponemes in the zones of election compared with the findings in controls. Contrary to previous reports the antisyphilitic activity of the impure penicillins was not shown to be superior to that of pure crystalline penicillin G in these animals. *James Marshall*

2699. **The Treatment of Acute Syphilitic Orchitis and Generalized Syphilis of Rabbits with Repository Penicillin Products Alone and in Combination with Mapharsen and Bismuth Salicylate**
J. A. KOLMER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 45–65, Jan., 1950. 18 refs.

Experimental syphilis in rabbits is much easier to cure than syphilis in human beings and less penicillin per kg. body weight is required, but data from experimental syphilis may nevertheless have some practical application in treatment of human syphilis. The author reports the results obtained with four repository penicillin compounds in 8-day and 15-day courses of treatment of acute syphilitic orchitis and generalized syphilis in rabbits inoculated with the Nichols–Hough strain of *Treponema pallidum*. The four compounds used were penicillin G sodium in refined peanut oil and bleached beeswax, procaine penicillin G in aqueous suspension, procaine penicillin G in sesame oil, and procaine penicillin G in refined peanut oil with 2% aluminium monostearate. Variations in curative activity were noted, probably due to the fact that the delaying action of the vehicle resulted in different levels of penicillin in blood; procaine penicillin G was found to be as effective therapeutically as penicillin G sodium in peanut oil and beeswax.

"Mapharsen" (oxophenarsine hydrochloride) by intravenous injection and bismuth salicylate intramuscularly were shown to have a synergistic action when combined with the penicillin compounds, this effect being greater with the arsenical. The author also states that iodides likewise show a synergistic action with penicillin compounds in rabbit syphilis, and believes that iodides by mouth should still be given in the latent and late stages of human syphilis. [The full details and results of these interesting experiments do not lend themselves to summarization.] *S. M. Laird*

2700. **Penicillin Treatment of Early Syphilis—First Four Patients After Six Years**
J. F. MAHONEY, R. C. ARNOLD, and A. HARRIS. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **30**, 350–355, Dec., 1949. 4 figs., 1 ref.

It is now more than 6 years since Mahoney and his colleagues made a preliminary report on the results of treating with penicillin 4 young seamen with early dark-field-positive syphilis. Three of these patients were given 48 injections of 25,000 units of penicillin at 4-hour intervals, and the fourth 85 similar injections. In one of the former gonorrhoea developed 273 days after treatment and he was given more penicillin (? 100,000 units). Thirty days later a dark-field-positive lesion appeared on the lower lip with a return of serum reactions to positive. Reinfection was diagnosed and he was re-treated with 60 3-hourly injections of 40,000 units of penicillin 318 days after his original treatment. It is of interest that this patient, a negro, had acquired gonorrhoeal infection (apparently treated with penicillin) 13 times by the 52nd post-treatment month.

Though the follow-up study of these patients was not so regular as might be desired, all four were recently brought under observation, when their clinical and serological condition, as well as that of the spinal fluid, was found to be completely normal. The authors consider that their apparent haste in using penicillin in human syphilis before its complete assay in the animal has been amply justified and they plead for more frequent pilot studies in human beings in those cases where the

product under scrutiny is known to be non-toxic and in which its trial would not jeopardize the chance of success of orthodox therapy should the experimental methods fail. *G. L. M. McElligott*

2701. **The Antitreponemal Effect of Oral Chloromycetin in 32 Cases of Early Syphilis in Man—A Preliminary Report**
M. J. Romansky, S. Olansky, S. R. Taggart, and E. D. Robin. *Science* [*Science*] **110**, 639–640, Dec. 9, 1949.

The authors treated 32 patients with early syphilis, confirmed by dark-field examination, with 8 to 56 g. of chloramphenicol given by mouth, usually in equal doses at 4-hourly intervals over a period of 4 to 6 days. Thirteen of the patients had secondary, and the remainder primary syphilis. The dark-field examination became negative within 22 to 28 hours of starting treatment and the healing of the lesions was prompt. Serological tests on 15 of the patients were positive before treatment; one month after completing treatment the reaction had become negative in one of these cases and was less strongly positive in the others. Nine of these patients were again tested after a further month, when the reaction in 2 others had become negative and improvement was maintained in the remainder. The observation is made that chloramphenicol appears to promote healing by a different mechanism from that of penicillin, the process being initiated from the base as opposed to the periphery of the lesions. *R. R. Willcox*

2702. **A Case of Gumma of the Lung.** (Un caso de sifilis gomosa pulmonar)
M. Sanchez-Barriga Carapeto. *Actas Dermo-Sifiliográficas* [*Actas dermo-sif.*] **41**, 147–149, Nov., 1949.

GONORRHOEA

2703. **Treatment of Gonorrhea with Oral Penicillin**
A. Jacoby and A. H. Ollswang. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 60–61, Jan., 1950. 1 ref.

A study is briefly reported of the treatment of gonorrhoea with penicillin by mouth in a New York clinic. There were 284 males and 25 females; infection was diagnosed by smear and culture, being acute in the majority of cases. Tablets of crystalline penicillin G buffered with glycerides and sodium salts of fatty acids or with aluminium hydroxide were used, the dosage ranging from 100,000 to 600,000 units. In many cases treatment was given as a single dose before the patient left the clinic. The disappearance of symptoms and the finding of three successive negative smears and cultures at weekly intervals were considered to represent a cure. When less than 400,000 units were given no cures resulted. When the dose ranged from 400,000 to 600,000 units, 82 to 84% of males and 72 to 100% of females were cured. Studies of penicillin level in the blood in these cases are recorded and it is believed that oral penicillin will prove "a practical, painless, and satisfactory therapeutic procedure". *S. M. Laird*

2704. **Treatment of Gonorrhoea in Women by the Local Submucous Injection of Penicillin; Control of Results by Gonococcal Culture.** (Traitement de la blennorragie féminine par les injections pénicillinées locales sous-muqueuses. Contrôle des résultats par la culture du gonocoque)
J. R. Debray. *Presse Médicale* [*Pr. méd.*] **57**, 1134–1135, Dec. 10, 1949.

This technique was developed as a result of the observation that the standard treatment of gonorrhoea by penicillin was much less effective in women than in men. With a fine dental needle, six to eight submucous injections of 1·5 ml. penicillin solution (500,000 units in 20 ml. saline) are made within the cervical canal. Four injections are given around the urethra, a surface analgesic being previously used. If there is evidence of infection of the glands of Skene or Bartholin, local injections are given. In the first instance treatment is given every other day for 8 days, but it may be continued if the results are not then satisfactory. Penicillin in aqueous solution (400,000 units in two doses, morning and evening) is also injected intramuscularly on the first and last days of treatment, and 3 g. sulphathiazole is given daily for the first 3 days. Results are controlled by cultures and have been markedly better than with standard treatment alone. *James Marshall*

2705. **The Use of Dihydrostreptomycin in the Treatment of Gonorrhea**
S. R. Taggart, D. E. Putnam, A. B. Greaves, and J. A. Watson. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 62–63, Jan., 1950. 3 refs.

Streptomycin in doses of 0·3 to 0·6 g. has cured gonorrhoea in some 90% of cases. Dihydrostreptomycin is here reported to have cured 95 out of 104 cases of gonorrhoea in the male when given as a single injection of 0·2 to 0·4 g. Smaller dosage was unsuccessful. Some transitory pain at the site of injection was the only reaction noted. *S. M. Laird*

2706. **Aureomycin in the Treatment of Gonorrhea in the Male**
R. C. V. Robinson. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 64–66, Jan., 1950. 6 refs.

Aureomycin promises to prove useful in all the venereal diseases. Earlier American reports indicated that it was effective in gonorrhoea, although to a lesser degree than penicillin; the present report confirms this view. Gonorrhoea in 77 males was treated with a single dose of aureomycin taken by mouth under supervision. The first 7 patients received 0·5 g. only and in 3 the treatment failed. The remaining 70 patients were each given 1 g. (four 250-mg. capsules) and 56 (80%) were considered cured. The urethral discharge abated within 10 to 24 hours. The author believes that re-infection and alcohol consumption may have been responsible for some failures, but that aureomycin given as described is less effective than 75,000 units of procaine penicillin in oil. *S. M. Laird*

Genito-Urinary Disorders

2707. **Oral Administration of Aureomycin in the Treatment of Urinary Infections**
A. M. RUTENBERG and F. B. SCHWEINBURG. *New England Journal of Medicine* [*New Engl. J. Med.*] **241**, 698–700, Nov. 3, 1949. 4 refs.

Aureomycin causes pain if it is injected intramuscularly, with or without procaine solution. However, the antibiotic is effective when given by mouth, as was demonstrated in the treatment of 26 patients suffering from acute or chronic urinary infections, in 17 of whom other antibiotics had failed to relieve the condition. A daily total of 2 g. of aureomycin was given in divided doses for a minimum of 4 to 6 days and until the causal organism had been eliminated from the urine for 2 or 3 days, but in no case for a period longer than 2 weeks. At the same time, appropriate measures were taken to relieve any obstruction in the urinary tract. There were a few cases of nausea and vomiting attributable to the antibiotic, which in 2 instances was severe enough for treatment to be stopped. On every second day, a catheter specimen of urine was cultured, the test of cure being taken as 2 to 5 consecutive sterile specimens.

According to this criterion, recovery took place in 19 cases. Urinary infection recurred in 3 of these patients, but further aureomycin therapy proved to be successful. Rapid clinical improvement resulted in all cases, usually in 24 to 48 hours and especially when the infecting organism was sensitive to aureomycin *in vitro*. Bacterial resistance did not develop during the course of treatment. Success was achieved in eliminating 12 strains of *Aerobacter aerogenes* from the urine, as well as 7 or 8 strains of *Bacterium coli*, 5 strains of *Pseudomonas aeruginosa*, and 1 strain each of *Proteus vulgaris*, haemolytic *Staphylococcus aureus*, and *Streptococcus faecalis*. Failures were recorded in 6 cases due to *Ps. aeruginosa* and in 1 case due to *Bact. coli*. It is noteworthy that sulphamezathine therapy was successful in 2 of these cases. *A. Garland*

2708. ***Aerobacter aerogenes* Infection of the Urinary Tract. Effective Treatment with Aureomycin**
S. F. WILHELM, W. A. SCHLOSS, L. A. ORKIN, E. SELIGMANN, and M. WASSERMANN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 837–839, Nov. 19, 1949. 5 refs.

In the Urologic Service of the Beth Israel Hospital, New York, a remarkable increase in the incidence and pathogenicity of *Aerobacter aerogenes* (*Bacillus lactis aerogenes*) infection of the urinary tract has been noted since 1948. Out of 100 consecutive admissions, the organism was found in the initial cultures in 50 cases and in later cultures in a further 25. Bacteriaemia was proved in 24 patients, of whom 7 died. This provides ample evidence that this organism is pathogenic in the genito-urinary tract and often gives rise to grave and sometimes fatal infection. Treatment with various drugs has been tried. Sulphathiazole cured 4 out of a series of 18 patients. Sodium mandelate, given intravenously, cured 40% of 43 patients, but administration was a troublesome procedure often resulting in phlebitis. Methenamine mandelate, given by mouth, gave more encouraging results: of 47 patients treated, 49% appeared to be cured after the prolonged administration (up to 5 weeks) of this drug. Aureomycin has, however, proved to be the most consistently efficacious drug. In a series of 50 cases the immediate clinical response was excellent in 42 (84%). There was, however, a high incidence of recurrence (43%)—in some instances as much as 2 months after the administration of aureomycin had been discontinued—though a further course of aureomycin sterilized the urine in most cases. It is considered that the action of aureomycin is bacteriostatic rather than bactericidal. No strain of the organism developed resistance to the drug, and no significant toxic symptoms were noted. The dosage recommended is 0·5 g. 4 times daily for 4 days, followed by 50 mg. 4 times daily for 4 days. *H. Stanley Banks*

2709. **Male Subfertility. Interim Report of 3,182 Cases**
H. A. DAVIDSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1328–1332, Dec. 10, 1949. 2 refs.

In 5,400 semen analyses the volume, density, total ejaculate, basic motility, and morphological abnormalities, both total and of the head only, were recorded. The technique of collection is described and a plea made for uniformity. There are many more factors in fertility than the actual quantity and quality of the semen, but by a consideration of the findings in 15 normal men and in 125 who were investigated for subfertility and subsequently impregnated their partners the author attempts to lay down minimal normal standards. He concludes that the common fault in cases of subfertility is abnormality of the spermatozoal heads. In these cases, even when pregnancy occurs it is likely to end prematurely. He condemns the practice of giving an opinion on a case without a complete analysis of a properly collected specimen of semen, as a reliable opinion can only then be given.

The results of treatment are not encouraging. Vitamin E and testosterone have been used but no improvement definitely due to the treatment has been obtained. Complete semen analysis is of value, however, if only for the fact that it saves patients with azoospermia and oligozoospermia from the inconvenience of treatment which can do them no good. In such cases testicular biopsy is essential. If complete lack of spermatogenesis is found further efforts are of no value. If normal spermatogenesis is found an obstruction of the vas or epididymis is certain and it may be possible to correct it by surgical treatment. Where spermatogenesis is merely delayed it may be hastened by treatment. A correlation of semen findings and testicular histology is likely to be of the greatest value in the treatment of cases of subfertility. *Thomas Moore*

Disorders of the Locomotor and Osseous Systems

2710. **Intravenous Amidopyrine Treatment, with Special Reference to Chronic Articular Rheumatism.** (Beitrag und Kritik zur intravenösen Pyramidonbehandlung unter besonderer Berücksichtigung des chronischen Gelenkrheumatismus)
W. H. FÄHNDRICH and J. JUNKERSDORF. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **74**, 845–848, July 15, 1949. 13 refs.

A carefully controlled attempt to confirm earlier reports of the beneficial effect in the treatment of rheumatoid arthritis of the intravenous administration of amidopyrine was carried out in 62 cases of acute and chronic forms of the disease, with an equal number of control cases. With either a 10% or 23·1% solution, it was found possible to give between 0·5 and 2 g. of amidopyrine daily, but only with great care under good clinical conditions. Vomiting, vertigo, and collapse (2 cases) were encountered, but no granulocytopenia. There was some improvement in the arthritis as shown by diminution of pain, increased mobility of joints, and lowered erythrocyte sedimentation rate, but the results in treated cases were not significantly better than in the controls. *Dushanka Wolstenholme*

2711. **Progesterone in the Treatment of Rheumatoid Arthritis. A Clinical Trial in 5 Cases**
W. R. M. ALEXANDER and J. J. R. DUTHIE. *Lancet* [*Lancet*] **1**, 297–298, Feb. 18, 1950. 12 refs.

Large doses of progesterone were administered to 5 patients with rheumatoid arthritis. No evidence of therapeutic benefit was obtained. No fall in the number of circulating eosinophils was noted after the injection of 100 mg. of progesterone. It is suggested that the remissions of rheumatoid arthritis which occur during pregnancy are not due to progesterone but may be attributable to increased production of other steroids by the adrenal cortex.—[Authors' summary.]

2712. **Haematological Changes in a Case of Rheumatoid Arthritis Treated with Adrenocorticotrophic Hormone (ACTH).** (Hematologiska förändringar hos ett fall av reumatoid artrit behandlat med adrenocorticotropt hormon (ACTH, corticotropin))
N. G. HÄVERMARK and N. G. NORDENSON. *Svenska Läkartidningen* [*Svenska Läkartidn.*] **46**, 2713–2719, Dec. 16, 1949. 4 figs., 5 refs.

A 62-year-old woman with a 6-months history of rheumatoid arthritis was treated with adrenocorticotrophic hormone (ACTH). The blood picture underwent the following changes. Haemoglobin value and erythrocyte count rose slightly, but fell at once after treatment. Serum iron level rose sharply during treatment but fell thereafter to its original level. The leucocyte count rose from 6,000 to 12,000 per c.mm. and then fell; the mononuclear count remained unchanged. The eosinophil count fell from 125 per c. mm. to *nil* during the first and from 272 to *nil* during the second course of treatment. Marrow puncture showed an improvement in the haematopoietic picture, which became temporarily almost normal. *B. Nordin*

2713. **A Study of the Albumin and Globulin Content in Postpartum Plasma and its Use in Rheumatoid Arthritis**
L. W. GRANIRER. *Science* [*Science*] **111**, 204, Feb. 24, 1950. 4 refs.

Pregnancy in patients with rheumatoid arthritis often results in a partial or complete remission (Hench, *Proc. Mayo Clin.*, 1938, **13**, 161). The author has observed a similar striking clinical improvement, lasting 3 to 16 weeks, in the local and general condition of patients treated by the administration of plasma obtained from mothers recently delivered. On estimating the protein content of 12 batches of such plasma, each containing the pooled plasma of 8 healthy donors without anaemia or oedema, a reduced concentration of albumin was consistently found, resembling that found in maternal serum at or near term (Moore *et al.*, *Amer. J. Obstet. Gynec.*, 1949, **57**, 312). The average total protein content was 4·35 mg. per 100 ml., that of albumin being 2·15 mg. per 100 ml. and of globulin 2·20 mg. per 100 ml.—an albumin–globulin ratio of 0·9. Although there is at present no clear explanation of the ameliorating effect of infusion of post-partum plasma in cases of rheumatoid arthritis, the author suggests that it may not be due solely to a steroidal factor. Further study of the mechanism involved is being undertaken. *D. I. Crowther*

2714. **The Serum Proteins in Rheumatoid Arthritis**
A. D. WALLIS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **32**, 63–71, Jan., 1950. 1 fig., 26 refs.

In order to provide an explanation of the tendency of severe typical rheumatoid arthritis to depress the serum albumin–globulin ratio, sera selected for their low ratios on the basis of chemical fractionation were subjected to more sensitive procedures. Electrophoretic analysis of samples from 4 patients confirmed previous observations of increases in the α (inflammatory response) and γ (antibody response) components, chiefly the latter. In addition 3 of the 4 showed a T component, not previously reported in rheumatoid arthritis serum. Less conspicuous in normal sera by the technic used herein, this fraction, like the γ component, is attributable to immunization. Examination of samples from 10 patients by an immunologic method, utilizing rabbit anti-human γ globulin serum, showed greatly increased γ globulin values, which averaged more than twice the normal content of this component.

In a discussion of the " hyper-immunity " of severe rheumatoid arthritis it is suggested (*a*) that the responsible antigen is not necessarily of infectious origin but

could be derived from the patient's own tissues, (*b*) that the antibodies serve no evident useful purpose, and (*c*) that for the sake of excessive antibody production the patient is apparently sacrificing his plasma albumin, his hemoglobin and his general tissue nutrition.

These data are interpreted as indicating that the hyperglobulinemia of active rheumatoid (atrophic) arthritis is the result of the combined effects of inflammation, tissue destruction and immunization, the last being the major contributor in all but the early stages of the disease.—[Author's summary.]

2715. **Preliminary Observations on the Antiarthritic Effect of 21-Acetoxypregnenolone**
J. SEIFTER, P. J. WARTER, and D. R. FITCH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **73**, 131–134, Jan., 1950. 2 refs.

The permeability of the synovial membrane of the rabbit to fluids is increased by hyaluronidase and desoxycorticosterone (deoxycortone) acetate (DOCA) and decreased by cortisone. 21-Acetoxypregnenolone is as active as cortisone in decreasing permeability: it also antagonizes the effect of DOCA and hyaluronidase on the synovial membrane. Seven ambulatory patients with active rheumatoid arthritis received intramuscular injections of 100 mg. of 21-acetoxypregnenolone on the first day, 200 mg. on the second day, and 300 mg. on the third day for a total period of 14 days. In all cases there was a reduction in swelling, lessening of pain, and increased mobility in the affected joints.

G. M. Findlay

2716. **Importance of Synovial Biopsy in Rheumatoid and Rheumatic Arthritis.** (Importancia de la biopsia de la sinovial en las artritis reumatoideas o reumaticas)
J. A. PIQUE and F. SCHAJOWICZ. *Revista Argentina de Reumatologia* [*Rev. argent. Reum.*] **14**, 154–162, Nov., 1949. 12 refs.

An account is given of the histological findings in synovial biopsy specimens taken from 12 patients with rheumatic arthritis. The authors consider the procedure to be especially helpful in those cases where other investigations have proved to be inconclusive, but it is contraindicated in cases of caseous tuberculous joint lesions or cold abscesses. *René Méndez*

2717. **Pituitary Implantation in Rheumatoid Arthritis.** (Hypofysinplantation vid kronisk artrit)
G. EDSTRÖM. *Nordisk Medicin* [*Nord. Med.*] **43**, 263–266, Nov. 11, 1949. 3 figs., 15 refs.

Following the introduction of adrenocorticotrophic-hormone treatment for rheumatoid arthritis, the author has resumed an experiment on which he originally reported in 1942. In 9 cases in which rheumatoid arthritis had been present for not more than 4 years calf or human foetal pituitary was implanted in September, 1949, and 6 of these patients have since been discharged without subjective or objective joint symptoms, with a low erythrocyte sedimentation rate (below 10 in all but one), and in good general condition. Increased mobility and reduced oedema were observed in the joints within 24 hours of the implantation, and subsequently the weight rose and the sedimentation rate fell. There was a fall in the eosinophil count and a rise in 17-ketosteroid excretion. The results were better in patients under the age of 40 than they were in older patients. *B. Nordin*

2718. **Epidemic Myalgia.** (La myalgie épidémique)
L. RONSE. *Bruxelles-Médical* [*Brux.-méd.*] **29**, 3411–3422, Nov. 20, 1949. 16 refs.

After reviewing the history and literature of epidemic myalgia the author gives a full account of the symptoms, signs, and treatment of the disease. He stresses the presence of headache, neck stiffness, and other neurological signs as important diagnostic features, and emphasizes the changes found in the cerebrospinal fluid. " Prontosil rubrum " was used in the treatment of the early cases and sulphadiazine in the later ones. In some cases a stock vaccine (" propidon ") gave dramatic relief.

The differential diagnosis from pneumonia and acute abdominal and other conditions is also discussed and the reasons for considering epidemic myalgia as a variant of poliomyelitis are examined. The author does not consider that there is sufficient evidence to prove that these diseases are caused by similar strains of virus but believes that epidemic myalgia is due to a virus which attacks the meninges.

The facts put forward in this paper are illustrated by references to 15 case histories collected over the past five years; in one case a biopsy examination was performed on a muscle nodule.

Kathleen M. Lawther

2719. **The Treatment of Osteo-arthritis by the Intra-articular Injection of Acid.** (Le traitement des arthroses par les injections acides intra-articulaires)
J. PARAF, A. ABAZA, and E. PERETZ. *Revue du Rhumatisme* [*Rev. Rhum.*] **16**, 609–613, Dec., 1949. 15 refs.

The authors describe in detail the technique and indications for the intra-articular injection of acid solutions which, they emphasize, should be used as a form of treatment only for post-traumatic arthritis and osteo-arthritis. Complications are stated to be uncommon, and mainly due to faulty technique. The solution recommended is 0·2% lactic acid and 0·5% procaine in isotonic saline.

The effect of the injection of the solutions is to produce immediate relief of pain and relaxation of muscle spasm, thus increasing the range of movement at the joint. Two cases are described in detail, and the authors state that of 40 patients thus treated marked improvement resulted in about 75%. [The joints affected and the length of observation are not stated.] Some cases [no details] were treated by injection of 1% procaine alone, and others by injection of a solution of monopotassium phosphate, but although some improvement was seen in these cases, it was concluded that the combination of procaine and lactic acid was more effective.

Kathleen M. Lawther

Neurology

2720. **An Electroencephalographically Localized Focus in a Case of Sturge-Weber Syndrome, Extirpated with Good Result.** [In English]
B. BROAGER and H. HERTZ. *Acta Psychiatrica et Neurologica* [*Acta psychiat., Kbh.*] **24**, 1–8, 1949. 4 figs., 6 refs.

Electroencephalographic studies alone made it possible to localize precisely the focus of epileptic discharge in a 5-year-old child suffering from the Sturge–Weber syndrome. The excision of the parasagittal premotor cortex and coagulation of the naevus found inside the dura in this region improved the patient's condition considerably. *J. T. Leyberg*

2721. **Studies in Disorders of Muscle. I. The Problem of Progressive Muscular Dystrophy**
F. H. TYLER and M. M. WINTROBE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **32**, 72–79, Jan., 1950. 24 refs.

A brief review of previous studies of progressive muscular dystrophy is presented. It is pointed out that two groups of progressive muscular dystrophy can be distinguished on clinical and genetic grounds: the childhood and facioscapulohumeral types. Dystrophy frequently is a genetically determined disorder. A peculiar pattern of muscular atrophy related to the age at which the anlage of a particular muscle appears in the embryo is found in progressive muscular dystrophy. Creatinuria is the only well documented anomaly of metabolism which has been discovered in the patient with progressive muscular dystrophy. No other data are available on which to start a search for the mechanism of the pathogenesis of this disease. A good argument for the existence of a specific biochemical lesion in the metabolism of the involved muscle can be developed.—[Authors' summary.]

2722. **Evaluation of Antiepileptic Drugs**
G. CHEN and C. R. ENSOR. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **63**, 56–60, Jan., 1950. 4 refs.

2723. **On Root Neuritis and Sciatica.** [In English]
S. EKVALL. *Uppsala Läkareföreinings Förhandlingar* [*Uppsala LäkFören. Förh.*] **54**, 397–428, Dec., 1949. 1 fig., bibliography.

The author tries to show that sciatica is not due to root compression alone, since compression can occur without pain. He believes that a non-specific infection occurs in the roots, and quotes the histological findings of others in support of his thesis. The local anatomical arrangement—deep root pockets in the lumbo-sacral segments and connexions between the meningeal spaces and radicular lymph channels—favours the localization of an infection at the level of the L5 and S1 roots. Moreover, the erythrocyte sedimentation rate is often raised and in some of his cases there was a history of preceding acute respiratory infection.

In 3 cases root section was performed because of intractable pain, and study of biopsy specimens revealed chronic non-specific neuritis with round-cell infiltration, especially in pericapillary areas. Case histories are given. Disk protrusion was not found in any. He considers that compression, usually from a disk, leads to nerve irritation, this being aggravated in the lumbo-sacral area by movement of bone over a relatively fixed nerve, and that infection subsequently localizes there with resultant sciatica. Sciatica is uncommon in the old because the joints are rigid, and uncommon in the young because disk protrusion is rare. Perhaps therefore a stabilizing procedure should be performed if laminectomy is undertaken.

The pain of sciatica is, he considers, at least partly sympathetic in origin; lumbar block may relieve the pain; coldness and hyperalgesia arise from vasoconstriction, and an intragluteal histamine injection gives a weak response on the affected side. Pain on sneezing or coughing may be due to sudden movement at the lumbar joints; the author has never been able to cause pain by jugular compression. [Naffziger's sign is not mentioned.]

[This is a long and largely theoretical paper. A long index to the literature is given, but few non-Continental authors are quoted.] *D. P. Jones*

2724. **Observations on the Treatment of Spastic Paralysis: Curarizing Alkaloids as an Adjunct to Physiotherapy.** (Contribution au traitement de la paralysie spastique: les alcaloïdes curarisants au service de la physiothérapie)
J. MICHAIL. *Presse Médicale* [*Pr. méd.*] **58**, 4–5, Jan. 7, 1950. 19 refs.

This paper describes encouraging results from the use of "intocostrin" as an aid in the physiotherapy of spastic paralysis in children. Of 17 cases treated, 11 had Little's disease, 5 infantile monoplegia or diplegia, and 1 a spastic paraplegia following myelitis.

The maximum dose of intocostrin used was 0·75 unit per kg. body weight, the initial dose being 0·5 unit per kg. The injections were given weekly. Improvement, sometimes considerable, was obtained in spasticity, adductor contractures, flexion deformity, and talipes equinus in 15 cases. Two cases remained unchanged. The results are tabulated.

The author states that this simple treatment greatly facilitates the work of the physiotherapist and minimizes the discomfort of the patients during treatment. It also for the most part does away with the need for surgical treatment of the deformities and for cumbrous orthopaedic appliances. *J. MacD. Holmes*

2725. **Intravenous Histamine in the Treatment of Nervous Disorders.** (Infusions intraveineuses d'histamine dans les maladies nerveuses)
M. Šercl. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 1247–1249, Dec. 24, 1949. 23 refs.

The effect of repeated intravenous infusions of histamine in various nervous diseases is described. At first histamine alone in doses of 1 mg. diluted with 500 ml. of physiological saline was infused slowly. Later the histamine was combined with 300 mg. of vitamin B_1 and 1 g. of vitamin C in 500 ml. of saline. The injections were repeated every 2 or 3 days in cases of disseminated sclerosis, familial cerebellar ataxia, muscular dystrophy, myotonia congenita, hemiparesis, and " other nervous disorders ". [The number of cases of each disease treated is not given.] The author states that this method of treatment produces amelioration of the pyramidal symptoms and muscular contractions, particularly in disseminated sclerosis, and speculates that the effect is produced by a hyperaemia around the lesions.

[The article is vague and unconvincing and has little to commend it.] *J. MacD. Holmes*

2726. **Prognosis in Disseminated Sclerosis**
M. Reinhold. *British Medical Journal* [*Brit. med. J.*] **1**, 160–162, Jan. 21, 1950. 2 refs.

The records were examined of 279 cases of disseminated sclerosis admitted to four homes for incurables in the London area and to the National Hospital, Queen Square, London, between 1880 and 1947, with the addition of 6 others obtained from other sources. Cases were grouped with regard to " onset of disability ", this being taken as the age at which symptoms caused some permanent disability or, if transient, were followed so shortly by other episodes as to leave little doubt about diagnosis. No statistical relation could be established between this age and the subsequent duration of the disease.

In the 57 cases in which necropsy was carried out the commonest secondary causes of death were disease of the respiratory system (45·5%) and disease of the urinary system (21·1%). *H. McC. Giles*

2727. **Meningo-ependymal Mycosis: Clinical and Anatomical Study.** (Mycose méningo-épendymaire. Étude anatomo-clinique)
R. Garcin, R. Martin, I. Bertrand, J. Gruner, and R. Tourneur. *Presse Médicale* [*Pr. méd.*] **57**, 1201–1204, Dec. 25, 1949. 6 figs., 42 refs.

2728. **Acute Lymphocytic Choriomeningitis. A Study of Twenty-one Cases**
W. R. Green, L. K. Sweet, and R. W. Prichard. *Journal of Pediatrics* [*J. Pediat.*] **35**, 688–701, Dec., 1949. 2 figs., 22 refs.

The authors report 21 proved cases of lymphocytic choriomeningitis of virus origin, 5 of the patients being under the age of 15. A suggestive seasonal incidence was noted, only 2 cases occurring in the summer, compared with 8 in the autumn and 7 in the spring. Association with mouse-infested houses was marked, and the virus was isolated from mice trapped in these houses. Headache was a constant symptom, nausea and vomiting were prominent, and photophobia was noted in 6 cases. Fever was present in all, as was neck stiffness; in 16 of the 21 cases Kernig's sign was positive. The authors stress the severity of the illness at the onset (only 6 of the patients were mentally clear on admission), and feel that the term " benign " commonly applied to the disease is apt to be misleading. Examination of the cerebrospinal fluid revealed a lymphocytosis of 90 to 100% with the total cell count ranging from 142 to 3,370 per c.mm. The protein content was raised (from 50 to 400 mg. per 100 ml.) and the sugar content generally reduced. The virus was grown in 15 cases; in the remaining 6 a rise in neutralizing antibody titre was observed. Examination of the blood showed a fairly normal total and differential leucocyte count. In the 4 cases in which the erythrocyte sedimentation rate was determined it was normal, the disease thus differing from tuberculous meningitis.

The differential diagnosis from other virus diseases, especially poliomyelitis, is discussed, and the importance of isolating the virus before accepting a diagnosis of lymphocytic choriomeningitis is stressed. All the 21 patients recovered and the only complication of note was persistent headache. In treatment, bed rest is the most important item, particularly in preventing subsequent headache. The authors advocate stay in hospital until the cerebrospinal fluid is normal, and then 4 to 6 weeks' bed rest at home. *W. F. Gaisford*

2729. **Caramiphen Hydrochloride (Panparnit) in the Treatment of Diseases of the Basal Ganglions**
D. Sciarra, S. Carter, and H. H. Merritt. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 1226–1229, Dec. 24, 1949. 17 figs., 15 refs.

The authors, working at Columbia University and the Montefiore and Presbyterian Hospitals, New York, have investigated the effects of " caramiphen " hydrochloride (" panparnit ") in 43 patients with extrapyramidal lesions. They review the history of belladonna treatment and point out its limitations. Therapeutic trials of newer drugs such as amphetamine, pyridoxine, pethidine, curare, " benadryl ", and " mephenesin " are mentioned and briefly reviewed. " Panparnit " was first described in 1946 in Germany, where it was used in the treatment of extrapyramidal disease in the same year and was favourably reported upon. The literature of subsequent reports is briefly analysed.

The maker's recommended dosage is 0·0125 g. three times daily, which is gradually increased over a period of 2 weeks to the point of tolerance, the total amount given not to exceed 0·55 g. After a thorough trial at this dosage the authors noted no benefit at all. It was therefore increased in some cases to 0·025 g. three times a day, with a further gradual increase over weeks or months to the point of tolerance, the total dosage never exceeding 0·8 g. Toxic effects were no more frequent or severe with these larger doses.

In a group of 28 cases of postencephalitic (17) and idiopathic (11) Parkinsonism, all the patients had

previously been taking belladonna, which was gradually withdrawn, being entirely eliminated only after 2 to 3 weeks. All the patients were informed that a new type of treatment was being tried. At an initial examination, the degree of rigidity and tremor was noted and a re-assessment was made and any subjective improvement noted at intervals of 2 to 7 days during treatment, which was continued for from 3 to 15 weeks.

Of the 28 cases of Parkinsonism, in none was any objective improvement noted; 7 patients felt better, but in only one case was this maintained. Of 6 patients with dystonia musculorum, 3 claimed mild subjective improvement without any objective alteration. Three patients with hereditary progressive chorea, 2 with bilateral athetosis, and 2 with familial tremors were treated without any subjective or objective improvement. One of 2 patients with hepatolenticular degeneration (Wilson's disease) showed slight, and the other more definite, subjective improvement, but neither showed any objective change. Intravenous administration of the drug (2 ml. of a 2% solution) was tried on 2 patients, but produced marked toxic symptoms. Even with oral administration, 37 of 43 patients had toxic symptoms, of which the most common and severe was vertigo. A fine analytical evaluation is made of the many external factors which may influence treatment and have to be considered when assessing the value of any therapy in such chronic diseases. The authors conclude that panparnit is not more effective than other drugs in general use for the treatment of diseases of the basal ganglia. *M. H. Pappworth*

2730. **Stellate Ganglion Block in the Treatment of Acute Cerebral Thrombosis and Embolism. Report of Forty-four Cases**

E. W. Amyes and S. M. Perry. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **142**, 15–20, Jan. 7, 1950. 4 figs., 17 refs.

This paper records the result of treating recent cases of cerebral thrombosis and embolism by infiltrating the stellate ganglion with 2% procaine solution. The work is based on the assumption that the intracranial circulatory disturbance is to an extent spread or maintained by impulses passing through the perivascular sympathetic nerves.

The stellate ganglion lies near the junction of the body and the transverse process of the 7th cervical vertebra. A point is determined about two fingerbreadths superior to the sternal notch, just lateral to the trachea and medial to the great vessels and the inner border of the sternomastoid. After skin infiltration, a 22-gauge needle without a stylet is inserted close to the edge of the trachea. The great vessels are retracted with the other hand. With the patient supine, the needle is directed posteriorly, perpendicular to the vertical axis of the vertebral column. The area to be infiltrated is near the lateral aspect of the 7th cervical vertebra. After bone is reached, aspiration is performed to determine whether a vessel, the lung, or the spinal canal has been entered. Ten ml. of 2% procaine hydrochloride solution is used to infiltrate the ganglion, and if this is successful a Horner's syndrome will be produced within one to 20 minutes.

A preliminary intramuscular injection of 2 grains (0·13 g.) of phenobarbitone sodium is given to all conscious patients, a necessary precaution because of the possibility that 200 mg. of procaine hydrochloride will cause a convulsion.

In the present study veins were entered in a few instances, but a further approach was then made without incident. In 1 case a small haematoma developed, probably due to accidental piercing of the vertebral artery, which runs near the stellate ganglion. However, the haematoma soon disappeared. Neither the pleural cavity nor the spinal canal was penetrated, and the likelihood of such an occurrence is believed slight. Before any patient was treated a lumbar puncture was performed to help to rule out an intracerebral haemorrhage.

Of 44 cases of varying types treated, 28 were considered improved. The most pronounced changes were an increase in alertness and an improvement in behaviour. The results were usually considerably better in those patients who received treatment within a few hours of onset. No person who was recovering was treated. The best results were in cases without a previous vascular accident and in cases of embolism. The sympathetic paralysis did not usually last for more than a few hours and block was therefore repeated in some cases, with benefit in the authors' opinion.

An attempt was made to compare in 7 cases the clinical state with the electroencephalogram, but there was only a moderate degree of correlation between them.

It is suggested that the stellate ganglion should be blocked daily for 4 days, and that trial be made with a longer-acting local analgesic. *N. S. Alcock*

2731. **Non-Traumatic Thrombosis of the Carotid Artery**

N. O. Ameli and D. W. Ashby. *Lancet* [*Lancet*] **2**, 1078–1082, Dec. 10, 1949. 4 figs., 12 refs.

Conspicuously more common on the left side and in males, non-traumatic thrombosis of the carotid artery occurs chiefly in the fifth and sixth decades; in the first two features it differs from thrombosis of the smaller intracranial arteries. Arteriosclerosis seems a common cause, and thrombo-angiitis obliterans accounts for some cases; polyarteritis nodosa and temporal arteritis are rarely responsible; a few cases are due to retrograde thrombosis from an intracranial aneurysm, but in many cases no cause is found.

The characteristic feature is the occurrence of repeated minor episodes of paresis or dysphasia with partial recovery before the final onset of a more severe hemiplegia or aphasia; loss of consciousness is unusual. The first may precede the final episode by hours or even years. The thrombus is usually situated about a centimetre above the bifurcation, but the intracranial part of the artery only may be affected. The external carotid branches are usually dilated.

Six cases are described, all in middle-aged men; the left artery was involved in 5. One patient had had a previous coronary occlusion, one had peripheral arteriosclerosis, and in one there was absence of pulsation in several peripheral arteries. None had significant hypertension, and none syphilis. In 5 cases there were

two or more episodes, one patient had a progressive hemiparesis, two had severe dysphasia, and one gave a history of a complete hemiplegia; he was the only one who had complained of headache, and had at one stage had subarachnoid bleeding; unfortunately in this case there was no filling of the internal carotid at arteriography and no direct proof that there was in fact a thrombosis of the internal carotid artery itself. One patient had occlusion of the central retinal artery, and one had slight blurring of the disks.

In 2 cases complete occlusion of the internal carotid was demonstrated at operation, in one case with occlusion of the external carotid also. In 3 cases the intracranial part of the internal carotid artery was narrowed and straightened, though obstruction was not complete. In 3 the external carotid branches were larger than usual. Air studies in 3 revealed slight atrophy, especially on the thrombosed side, in 2. The electroencephalogram was grossly abnormal on the affected side in the 2 cases so examined. *J. Foley*

2732. **Thrombosis of the Internal Carotid Artery**
T. G. I. James. *British Medical Journal* [*Brit. med. J.*] **2**, 1264–1267, Dec. 3, 1949. 3 figs., 16 refs.

The author briefly reviews the literature on this subject and concludes that thrombosis of the internal carotid artery is not an infrequent cause of neurological disturbance.

Three cases of internal carotid thrombosis are reported in detail. In the first case there was a relatively sudden onset of symptoms; in the second case the onset was gradual over a period of 2½ years; in both these cases there was an internal carotid thrombosis just above the carotid bifurcation. In the third case there was sudden onset of hemiplegia associated with subarachnoid bleeding; later an intracerebral haematoma was discovered and evacuated. Angiography in this case showed a thrombosis of the internal carotid just above the carotid bifurcation in the neck.

The author emphasizes that the onset of this condition is usually sudden, and that the carotid syndrome of contralateral hemiplegia with associated thrombosis of the ophthalmic artery seems to be rare. He suggests that a slower onset is less common but in such a case a space-occupying lesion may be simulated. The aetiology of the condition is considered, and the author concludes that this still remains obscure. *E. B. C. Hughes*

2733. **Aneurysm of the Intracranial Carotid Artery. Syndrome of Frontal Headache with Oculomotor Nerve Paralysis**
R. Jaeger. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **142**, 304–310, Feb. 4, 1950. 3 figs., 19 refs.

Thirty-one consecutive cases of aneurysm of the intracranial carotid artery with the common symptoms of unilateral, orbital and frontal headache and/or involvement of the 3rd cranial nerve have been analysed in sufficient detail to point out the general pattern of these two symptoms. Other commonly associated observations, such as generalized headache, meningismus, mental disturbances, involvement of the other cranial nerves, and particularly of the 4th and 6th, are emphasized. The value of radiographic study after injection of a contrast medium in permitting a precise diagnosis and disclosing the shape, size and possibility for a reasonably safe surgical cure of the aneurysm would appear to be considerable from this series.

Five patients died (25%) after a craniotomy approach made in an attempt to specifically treat the aneurysms. This would not appear to be a prohibitive mortality in view of the probable serious outcome of these cases if the patients were untreated and in light of limited past experiences to guide the surgeon in this relatively newly recognized group of surgical lesions.

The following conclusions are to be drawn from this report: first, all persons of adult age with a persistent frontal or orbital pain or ache, associated with a 3rd nerve paresis or paralysis, should be suspected of having an aneurysm of the intracranial carotid artery. With these symptoms, arteriography is indicated in every instance to confirm the diagnosis and to determine the feasibility for direct surgical treatment. Second, most of these patients can be relieved or cured by specific surgical procedures without great or unnecessary risk.—[Author's summary.]

2734. **Effect of Change of Position upon the Cerebral Circulation of Man**
H. A. Shenkin, W. G. Scheuerman, E. B. Spitz, and R. A. Groff. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 317–326, Dec., 1949. 3 figs., 7 refs.

The cerebral circulation and metabolism in unanesthetized humans was studied in the supine position and after tilting either head up or head down 20°. In physiologically normal individuals tilting head up 20° does not change the cerebral blood flow, it being maintained in the face of a fall in carotid blood pressure by a reduction in cerebrovascular resistance. Tilting head down 20° slightly reduced the cerebral blood flow, in spite of an increase in carotid blood pressure. An increase in cerebrovascular resistance in the head-down position explained the lack of increase, and indeed decrease, of the cerebral blood flow in the head-down position.

The possible mechanisms causing the changes in cerebrovascular resistance in the above circumstances are discussed. The best correlation of changes in the cerebrovascular resistance with changes of position was obtained with the calculated changes in intracranial cerebrospinal fluid pressure.

Patients with brain tumours were studied in the supine position and after tilting head up or head down 20°. The mechanisms for adjustment when tilting these patients head up 20° failed and the cerebral blood flow decreased (30%). Tilting the brain tumour patient head down did not alter the cerebral blood flow. It is therefore concluded that the head-up position in the treatment of patients with brain tumour and/or increased intracranial pressure is deleterious; the use of the head-down position in the treatment of such patients does not appear to alter the cerebral blood flow.—[Authors' summary.]

Psychiatry

2735. **Studies on Adrenal Cortical Function in Certain Psychoses.** (Ricerche sulla funzionalità cortico-surrenale in alcune malattie mentali)
A. JARIA. *Folia Endocrinologica* [*Folia endocrinol., Pisa*] **2**, 605–613, Dec., 1949. 16 refs.

In 1948 Thorn *et al.* (*J. Amer. med. Ass.*, **137**, 1005) suggested the testing of adrenal cortical function by injection of adrenal corticotrophin. Among the results of such injection in the normal individual there is a diminution in the number of circulating eosinophils (or rather a particular type of neutrophils staining with a special eosin solution).

The author studied the eosinophil count after intramuscular injection of 15 mg. corticotrophin into 50 fasting psychotic patients, with mental disease of various origins, and 10 normal persons. Whereas the count fell by 30% of its initial value in all the latter, only 40% of the psychotic patients gave such a response, and in all cases of alcoholic psychosis, narcotic psychosis, and general paresis there was no fall in eosinophil count.

It is therefore suggested that mental disease is often associated with deficient adrenal cortical function.

S. S. B. Gilder

2736. **Disturbances of Bladder Function Associated with Emotional States**
L. R. STRAUB, H. S. RIPLEY, and S. WOLF. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 1139–1143, Dec. 17, 1949. 6 figs., 5 refs.

In an experimental study of the relation of bladder function to emotional stress, 27 patients with bladder disorders—urinary frequency, urgency, and retention—were chosen from hospital wards; there were 14 males and 12 females, ranging in age from 21 to 57. Each patient was subjected to full physical investigation: in none was any abnormality found which could account for the bladder symptoms. A detailed psychiatric history was taken in each case, and this material was supplemented where necessary by dream analysis, interview under "amytal" narcosis, and psychological testing of the projective type. By means of a calibrated cystometer with tambour recording device, records were made of changes in bladder pressure continuously over periods of 1 to 1½ hours, during which the patient was interviewed and topics known to be disturbing to him introduced. In many cases the urinary symptoms were associated with other somatic manifestations, such as headache and backache.

Of 18 patients who complained of frequency and urgency the occurrence of symptoms in all could be correlated with events presumed to be associated with serious personal conflict. In 7 of these a marked and sustained increase in bladder pressure was observed in the experimental interview when the relevant topics were discussed. In the other 11 cases no bladder changes were recorded, nor did the patients show any other sign of distress during the discussion. In 8 other cases there was urinary retention, with a large bladder capacity and reduced motor activity, associated with emotional conflicts and varying with changes in emotional state and life situation, while one patient suffered from alternating frequency and retention. [The cystometric findings in these cases are not reported.] In this case, the patient's usual response to stress was to develop frequency. On one occasion she was exposed to a sexual threat and felt desperate; shortly afterwards she found herself unable to urinate and required catheterization for the next 16 days. Both types of reaction may thus be found in the same subject.

In general, bladder hyperfunction with frequency was correlated with anxiety and resentment accompanying a conflict which was usually overt. Bladder hypofunction with retention of urine was found in reactions of withdrawal and defeat, with evidence of emotional repression. Aggressive behaviour was more commonly found in the former, and non-aggressive behaviour in the latter type of case.

[The methods used in this study are well described, but the conclusions are stated only in general terms and the detailed results of investigation in each patient are not given.] *Desmond O'Neill*

2737. **Rorschach Pattern in Duodenal Ulcer**
A. KALDEGG and D. Ó'NEILL. *Journal of Mental Science* [*J. ment. Sci.*] **96**, 190–198, Jan., 1950.

2738. **Kleptomania in Males.** (Über Kleptomanie beim Manne)
V. BAER-HESS. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **116**, 224–250, Oct., 1949. Bibliography.

The author makes an extensive survey of the literature dealing with the problem of kleptomania. She gives a detailed clinical account of one male case and discusses the different psychopathology in kleptomanic men and women.

Kleptomania is a rare condition in adult males and two types of case can be distinguished. Usually the male kleptomaniac is a fetishist, and the nature of the objects stolen shows a symbolical libidinal gratification. In the second group—to which the author's patient belonged—the psychopathology is not unlike that of female kleptomania. Obsessional-compulsive trends and latent homosexuality are predominant. In this group there is as a rule evidence of emotional immaturity, and the patient displays, both physically and mentally, strong feminine traits, resembling the typical female kleptomaniac in that the choice of object is of no importance and the act of stealing itself leads to the discharge of sexual tension. The paper contains a valuable bibliography of this fascinating subject.

J. T. Leyberg

2739. **Initial Clinical Experience with Antabuse**
F. GELBMAN and N. B. EPSTEIN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **60**, 549–552, June, 1949. 8 refs.

Experiences with the treatment of 55 cases of alcoholism by means of " antabus " (tetraethyl thiuram-disulphide) at the Allan Institute of Psychiatry, Montreal, are described. The method of administration was the orthodox one; of the 55 patients 45 have not reverted to their old drinking habits [the follow-up period being apparently a matter of weeks].

The following points seem worthy of note. The usual relation of individual patient to physician must be slightly altered, co-operation with a relative, friend, or social worker being desirable. The patient should at all times carry a card on him stating briefly that he is taking the drug, that reactions will occur with alcohol intake, and that in such an event contact should be made with the physician undertaking treatment. The only dangerous reaction occurred in a diabetic who, while taking 0·5 g. antabus daily but no alcohol, suddenly went into convulsions followed by loss of consciousness and hemiparesis. The drug appears to be contraindicated in diabetes. Other symptoms complained of during therapy may be the result of sobriety and not of the drug. Skin rashes appeared in 3 cases but yielded rapidly to " pyribenzamine " therapy without stopping the antabus.

S. S. B. Gilder

2740. **Death Following the Ingestion of Alcohol in an Antabuse Treated Patient**
R. O. JONES. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **60**, 609–612, June, 1949. 3 refs.

Very severe reactions as a result of alcohol ingestion during " antabus " therapy have already been reported by Bell and Smith (*Canad. med. Ass. J.*, 1949, **60**, 286). The present author now describes a case in which death followed the drinking of one ounce (28 ml.) of rum containing 43·3% of ethyl alcohol by volume. The patient, a young man without apparent organic disease, had received 5·5 g. of antabus over 5 days before drinking the rum. After a fairly severe reaction, including vomiting but otherwise of the type described by other authors, he died quite suddenly about 2½ hours after taking the rum. At necropsy acute congestive right-sided cardiac failure was found.

The alcohol concentration in blood was low (30 mg. per 100 ml.) but the acetaldehyde level was extremely high (0·86 mg. per 100 mg.). Why the latter level was so high and whether this was related to the fatality remains a mystery.

S. S. B. Gilder

2741. **Electric Shock Treatment of Psychosis in Pregnancy.** (Traitements psychiatriques de choc et grossesse)
M. POROT. *Presse Médicale* [*Pr. méd.*] **57**, 1118–1120, Dec. 3, 1949. 7 refs.

The author has collected 6 cases from the literature, and adds 3 of his own, in which shock treatment for psychiatric disorders was applied during pregnancy.

The shock in one case was induced with insulin, in another case insulin and electric shock were combined, and in the remainder electric shock alone was used. The age of the patients thus treated ranged from 22 to 33 years, the number of shocks from 3 to 30, and the duration of treatment from 3 to 8 months. In the 2 cases treated with insulin shock one patient had 23 and the other 33 comas. In one of these 9 cases abortion occurred 18 days after electric shock treatment, but following trauma unconnected with the treatment and sufficiently severe to account for the miscarriage. Two other cases of abortion after electric shock treatment are mentioned in the literature but, being referred to as " pathological pregnancies ", are excluded from this series. In all other cases the pregnancy terminated uneventfully for mother and child. As the number of cases published is still small—though the number of cases actually treated is probably much greater—the author recommends caution in the application of this form of therapy in pregnancy. It should be undertaken only when the psychiatric symptoms are likely to benefit by the treatment (as in depressive and manic conditions) and when the psychosis endangers the normal evolution of pregnancy (as in severe agitation or rapid general deterioration), and only in consultation with a gynaecologist. The wisdom of the author's cautious attitude is emphasized by reference in a footnote to a report by Gralnick of the death of the foetus in the last month of pregnancy in 2 cases after combined shock treatment; the publication of this report came to the author's notice only after he had completed his paper.

R. Klein

2742. **Comparison and Estimate of Group and Individual Methods of Treatment**
A. S. THORLEY and N. CRASKE. *British Medical Journal* [*Brit. med. J.*] **1**, 97–100, Jan. 14, 1950. 8 refs.

In this paper a comparison is made between the results of group psychotherapy and those of individual psychotherapy in comparable series of patients admitted to the Belmont Hospital between August, 1946, and December, 1948. The presenting feature of the diagnosis was used in classifying the cases, in which some overlapping necessarily took place. The clinical results were assessed by means of a questionary sent to each patient 3 months after discharge, to which replies were received from 216 out of the 291 patients treated, the highest proportion of failures to reply being in cases of psychopathic personality and schizophrenia. Group therapy consisted of lectures and discussions, educational subjects giving place to psychotherapeutic subjects as the experiment advanced, the activities of each group being left more and more to the patients themselves to decide. Individual therapy was superficial and non-analytical, the patients usually being seen twice a week. Some physical methods were used in the treatment of both groups, but the chief emphasis was on psychotherapy. The results in the two groups were not significantly different except in the case of depressive patients, who responded better to group than to individual therapy. Psychotherapeutic methods gave definitely better results than simple routine care. Increasing age, length of illness, and the presence of coincident physical organic disease were unfavourable influences on the response to psychotherapy.

R. G. Gordon

Infectious Diseases

2743. **Recovery of *C. burnetii* from *H. savignyi* Collected in Spain**
R. R. PARKER, J. DE PRADA, E. J. BELL, and D. B. LACKMAN. *Public Health Reports, Washington* [*Pbl. Hlth Rep., Wash.*] **64**, 1616–1618, Dec. 16, 1949. 1 ref.

Two groups of the tick *Hyalomma savignyi* were sent from the province of Salamanca, Spain, to the U.S.A. where *Rickettsia* (*Coxiella*) *burnetii* was isolated from the ticks, and infected guinea-pigs. *G. M. Findlay*

2744. **Rickettsialpox. Clinical and Laboratory Study of Twelve Hospitalized Cases**
L. P. BARKER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 1119–1123, Dec. 17, 1949. 3 figs., 7 refs.

The author reports 12 cases of rickettsialpox, giving a detailed description of one. The disease was discovered in 1946 in four districts of New York, and 150 cases have been recorded yearly. The organism has been identified as *Rickettsia akari* and has been recovered from the common house mouse (*Mus musculus*) and from rodent mites (*Allodermanyssus sanguineus*). The latter have been found as ectoparasites of the house mouse. The diagnosis is based on three characteristics, namely, (1) the initial lesion, caused by the bite of the rodent mite; (2) the symptoms—fever, sweats, severe headache, and general discomfort; (3) a papulo-vesicular eruption. The general symptoms start 2 to 7 days after the appearance of the initial lesion and the rash appears from 1 to 10 days after the first systemic manifestations. The diagnosis can be confirmed by the complement-fixation test during the acute illness and during convalescence; the leucocyte count usually shows a leucopenia with relative lymphocytosis and presence of some large monocytes, but in some cases a leucocytosis is found. The erythrocyte count and the haemoglobin index are within normal limits. The author enumerates the various diseases, such as chickenpox, smallpox, typhoid fever, infectious mononucleosis, and typhus, with which rickettsialpox may be confused. *Franz Heimann*

2745. **An Epidemic of Q Fever at Ravarino di Modena.** (Un focolaio epidemico di febbre "Q" a Ravarino di Modena)
M. COPPO, R. BERTOLI, and C. ZANUSSI. *Minerva Medica* [*Minerva med., Torino*] **2**, 863–868, Dec. 8, 1949. 3 figs.

2746. **Bone Involvement in Cryptococcosis (Torulosis)**
V. P. COLLINS. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 102–112, Jan., 1950. 9 figs., 35 refs.

The causative organism of cryptococcosis is *Cryptococcus neoformans*, also termed *Cryptococcus hominis* or *Torula histolytica*. It belongs to the group of fungi imperfecti. Both in the tissues and in culture it appears as encapsulated, rounded, budding cells, producing no mycelia or spores, and has been frequently mistaken for lymphocytes or erythrocytes.

In a review of over 200 cases of cryptococcosis reported in the literature bone was found to be involved in 17; three additional cases confirmed by radiography are reported. The lesions, when multiple, are widely disseminated and tend to involve bony prominences. They are usually osteolytic with little bone reaction. Changes occur slowly and both progression and regression have been observed. The radiographic appearances resemble more closely those of blastomycosis (due to *Blastomyces dermatitidis*) and coccidioidosis than those of actinomycosis.

Attention is drawn to the reported cases of cryptococcosis associated with histopathological changes indicating Hodgkin's disease and sarcoid. *A. Orley*

2747. **Nocardiosis, with a Report of Three Cases of Actinomycosis due to *Nocardia asteroides***
F. C. TUCKER and E. F. HIRSCH. *Journal of Infectious Diseases* [*J. infect. Dis.*] **85**, 72–86, July–Aug., 1949. 8 figs., 46 refs.

After a discussion of the literature, the authors describe 3 cases, 2 fatal, of *Nocardia asteroides* infection.

In the first case, 6½ months after sustaining a wound of the right thigh, which suppurated and in which numerous sinuses developed, the patient showed symptoms and signs of a cerebral abscess. Exploration revealed a deep left occipital abscess; this was aspirated, but the patient died. Post-mortem examination showed only the granulating wound in the thigh and chronic abscesses in the left occipital and right frontal lobes. Cultures of thigh wound and occipital abscess yielded *Nocardia asteroides*.

The second case began with a granulomatous infection of the nose and throat, with suppurative involvement of the submaxillary lymph nodes, the infection being resistant to penicillin, sulphadiazine, and hot packs locally. Later pleurisy developed and finally a fatal bronchopneumonia. The duration of illness was 8 months. Post-mortem examination showed subacute and chronic organizing bronchopneumonia, with multiple ulcers in the trachea, left bronchus, and intestine. Filaments were seen in sections of the affected tissues, and from lung and peritoneal, pericardial, and pleural fluid *Nocardia asteroides* was recovered. The third case began with extraction of a wisdom tooth; 3 months later a mass appeared in the neighbourhood of the right mandible and increased rapidly in size; it was incised and drained. *Nocardia asteroides* was grown from the pus. After some months healing occurred, but was followed by recurrence for which incision was needed, after which the patient appeared to recover.

The authors draw attention to the high variability in

some properties (such as acid-fastness) of *N. asteroides* and suggest a number of tests by which it can be recognized. *C. L. Oakley*

2748. **Oral Penicillin Prophylaxis of Recurrences of Rheumatic Fever. Interim Report on Method After a Three Year Study**
K. H. KOHN, A. MILZER, and H. MACLEAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **142**, 20–25, Jan. 7, 1950. 12 refs.

A study of the effect of oral penicillin in preventing recurrences of rheumatic fever was carried out on 126 children in a special school in Chicago for cases of rheumatic heart disease. The subjects were divided into two groups, comparable as to sex, race, age, and economic level, one being used as a control. A further control group of 80 children at another similar school were selected in the same manner, but were not in contact with those undergoing prophylactic treatment.

Penicillin was given in the hope that it might be possible thus to eliminate haemolytic streptococci and so to prevent or lower the incidence of rheumatic fever. For the former purpose, throat swabs from all the groups of children were examined at intervals during the course of treatment. At the end of 4 months' treatment with 50,000 units of penicillin twice daily, throat swabs showed no improvement in the treated group.

As it was thought that this dosage might be causing penicillin-resistance in the organisms the dosage of penicillin was changed to 1 mega unit daily for 5 days, repeated five times in the school year. This was found to cause a maximum reduction in streptococci in throat swabs from the treated children lasting for at least 3 weeks after the short course.

As a result, in the third year of the experiment, treatment was given in the first week of each calendar month throughout the school year and consisted of 200,000 units 4 times, or 250,000 units thrice, daily for 7 days. With this dosage the penicillin-treated group showed a consistently lower infection rate than did the control group from the same school. Owing probably to the lessened cross-infection risk, the latter group showed a markedly lower infection rate than did the group from the second school, in which the rate was similar, on the one occasion of comparison, to the rate among children in an ordinary school.

The recurrence rate of rheumatic fever in each of the 3 years remained steady at about 20% in the school where there was no prophylaxis. In the school with prophylaxis the rate among those given penicillin was consistently less than in the control group, though of doubtful significance in the first and second years. In the third year, however, there were no recurrences among the treated children, as compared with 11% among the untreated. This is regarded as a highly promising result.

During the second and third years, while penicillin was being given in larger doses for short periods, there was no evidence of the development of penicillin resistance among haemolytic streptococci of group A, B, or C in a total of 274 strains examined.

Reginald St. A. Heathcote

VIRUS INFECTIONS

2749. **Infection of Cattle with Vaccinia.** (Besmetting van het vee met vaccinia)
A. L. NOORDAM. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 4190–4191, Dec. 10, 1949.

A description is given of cases of cowpox (vaccinia) occurring in cattle infected by a recently vaccinated person, the vaccination being in the eruptive phase. Brothers of this young man were then (spontaneously) vaccinated by the infected udders of the cows. Cowpox is dangerous in that it may give rise to spontaneous vaccination in young milkers, with a risk of post-vaccinal encephalitis. *J. W. Tesch* (*Excerpta Medica*)

2750. **Action of Aureomycin and Chloromycetin on the Virus of Primary Atypical Pneumonia**
M. D. EATON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **73**, 24–29, Jan., 1950. 14 refs.

Primary atypical pneumonia in man responds to aureomycin (Schoenbach and Bryer, *J. Amer. med. Ass.*, 1949, **139**, 275; Kneeland *et al.*, *Amer. J. med. Sci.*, 1949, **6**, 41; Finland *et al.*, *New Engl. J. Med.*, 1949, **240**, 241; and Meiklejohn and Shragg, *J. Amer. med. Ass.*, 1949, **140**, 391). Aureomycin given intraperitoneally to cotton-rats starting 24 hours after intranasal infection with the virus of primary atypical pneumonia inhibits almost entirely the development of pulmonary lesions in a daily dose of 1 mg.: it is partly active in a dose of 0·5 mg. daily. Therapeutic activity is also demonstrable when treatment is delayed for 5 or 6 days with a daily dose of 2 to 5 mg. daily. Aureomycin inhibits the growth of the atypical-pneumonia virus in chick embryos when injected into the yolk sac in two doses of 1 mg. each 2 and 48 hours after amniotic inoculation of the virus. Chloramphenicol ("chloromycetin") in doses of 5 to 20 mg. per day has slight and irregular effects on the virus in cotton-rats. *G. M. Findlay*

2751. **Herpes Zoster. Treatment of Pain with Dehydroergotamine-45**
F. C. COMBES, O. CANIZARES, and S. SIMUANGCO. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **14**, 53–56, Jan., 1950. 5 refs.

A study of results obtained in the treatment of 40 cases of herpes zoster with pain shows that "dehydroergotamine 45" [dehydroergotamine methanesulphonate] controlled the pain in 30 of 40 patients (75%). In 17 instances the results were classified as "excellent" and in 13 as "satisfactory". There were 10 "failures". These included one patient with leukemia, one with primary pulmonary carcinoma with metastases, and 4 with post-herpetic pain of protracted duration. The location and duration of the eruption did not influence response to therapy except in instances of long standing post-herpetic pain. The clinical course of the eruption was not affected by the medication. In those instances where treatment was started early, new crops of vesicles often appeared after the first injection. In most patients

these vesicles dried in an average of one to two weeks. There was no appreciable advantage in intravenous administration except that results were more prompt. In most cases the intramuscular route was satisfactory. The dose of 1 cc. was found to give good results, but when it failed a larger dose (2 to 3 cc.) was often successful. The duration of relief from pain varied from 8 hours to 4 days. There were no serious side-effects.—[Authors' summary.]

2752. **Epidemic Apoplexy and Poliomyelitis. A Contribution to the History of Infantile Paralysis**
R. R. SCOBEY. *Archives of Pediatrics* [*Arch. Pediat.*] **67**, 29–46, Jan., 1950. Bibliography.

Although it has often been stated that poliomyelitis appeared in epidemics only 50 or 60 years ago, there is evidence that the disease has existed for centuries. Prior to 1890—59 years ago—poliomyelitis was reported from at least 24 different countries by more than 100 different names. There is evidence that poliomyelitis was known to the ancient Egyptians; it was apparently described by the early Greek writers under the name of apoplexy. This term, or various modifications of it, was applied until the nineteenth century to paralytic manifestations occurring during seasons when epidemics of poliomyelitis are known to occur.

The term heat-apoplexy, which often resulted in manifestations similar to those of encephalitis and poliomyelitis, was also formerly applied to epidemics of disease appearing during hot seasons. The incidence of sunstroke has decreased during recent years, whereas the incidence of cases of poliomyelitis has increased and has involved older age groups. This paradoxical situation suggests that cases formerly designated as heat-apoplexy, sunstroke, etc., are now classified as poliomyelitis. The criteria for the diagnosis of poliomyelitis, viz., the presence of an epidemic, fever, rigidity of the spine, pleocytosis, and paralysis were not infrequently present in the cases of heat-apoplexy described by early writers. —[Author's summary.]

2753. **Use of Complement Fixation in the Differentiation of Strains of Coxsackie Virus**
B. F. HOWITT and U. R. BENEFIELD. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **73**, 90–92, Jan., 1950. 5 refs.

The Coxsackie viruses isolated in America can be differentiated by the use of the complement-fixation test (Casels *et al.*, *Proc. Soc. exp. Biol., N.Y.*, 1949, **72**, 636). Observations now demonstrate that there are at least five types: complement-fixation tests show agreement with virus-neutralization tests. Complement-fixing antibodies are present by the fourth day after onset.

G. M. Findlay

2754. **Trial of Cortin in the Treatment of Poliomyelitis.** (Une nouvelle tentative de traitement de la poliomyélite: la cortine extractive)
L. BINET, M. LANGUILLE, P. TANTRET, and P. VERNANT. *Progrès Médical* [*Progr. méd., Paris*] **77**, 563–567, Dec. 24, 1949. 5 figs.

2755. **The Treatment of Infective Hepatitis with Adrenal Cortical Hormone.** (Ueber die Behandlung des parenchymatösen Ikterus mit Nebennierenrindenhormon)
P. BÜCHMANN and H. SCHULZE-BUSCHOFF. *Medizinische Klinik* [*Med. Klinik*] **44**, 881–888, July 15, 1949. 2 figs., 31 refs.

A series of 25 patients with infective hepatitis were given intramuscular injections of deoxycortone (desoxycorticosterone) acetate, 40 mg. in oil and 50 mg. of a crystal suspension on the 1st day, and 30 mg. in oil on the 2nd and 3rd days. Other treatment consisted of rest, warmth, low-fat high-carbohydrate diet, 50 g. of dextrose in drinks daily, and restriction of salt intake to 5 g. daily. In 22 cases there were marked clinical improvement and rapid fall in serum bilirubin level. Two patients who also had diabetes did particularly well. No toxic effects were noted; there was temporary increase in weight and occasional slight oedema, but no rise in blood pressure. The authors recommend this treatment especially for cases in which there are no signs of improvement in the 3rd or 4th week of the disease.

Dushanka Wolstenholme

2756. **Cultivation of Mengo Encephalomyelitis Virus in the Embryonated Hen Egg**
G. W. A. DICK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **73**, 77–80, Jan., 1950. 12 refs.

A number of the encephalo-myocarditis viruses (Columbia SK, MM, and EMC viruses) have been grown in the embryonated hen egg: experimental evidence is given to show that Mengo encephalomyelitis virus also grows in the chick embryo, which is killed within 48 to 96 hours of inoculation with widespread degenerative changes and haemorrhages throughout the embryo.

G. M. Findlay

2757. **Management of the Common Cold with Neohetramine (Anahist). A Preliminary Report**
H. E. TEBROCK. *Industrial Medicine* [*Industr. Med.*] **19**, 39–41, Jan., 1950. 17 refs.

The author, who is medical officer to a large electric company in New York, cites the common cold as an important cause of loss of work and wages. He reviews the use of antihistamine drugs in the treatment of upper respiratory infections and quotes the view that 8 out of every 10 persons susceptible to colds are either themselves allergic, or have a family history of allergy. He believes that the symptoms of the common cold are allergic manifestations to the cold virus and are associated with increased histamine formation. "Anahist" ("neohetramine") is reported to give rise to less dizziness, sleepiness, and other side-effects than other antihistamine drugs. The suggested dose of 50 mg. 4 times a day was, however, found to cause toxic symptoms too frequently to be safe, and the therapeutic results were as good and toxic symptoms rarer if the dose was halved. This dose (25 mg. 4 times daily) was given to 782 workers as a prophylactic against the common cold for at least 6 weeks and to some for 3 months. Only 25% of this group developed colds, whereas 65% of a control group

of 250 who were given placebos suffered from colds during the same period. Moreover, in those of the former group who developed colds, the symptoms were less severe and lasted on average only 2 to 4 days, "contrasted with 7 to 9 days in the same individuals taking their usual remedies". Of 963 workers with colds of less than 48 hours' duration who were given anahist in the same dosage, 83% reported complete alleviation of symptoms within 2 days. Only 2·5% of the total of 1,745 persons who took the drug suffered from toxic symptoms. The author concludes that anahist is a very useful drug in the prophylaxis and treatment of the common cold.

[The view that the common cold symptoms are allergic and associated with excess histamine formation makes nonsense of orthodox conceptions of allergy. If the symptoms are allergic, what are the more usual symptoms produced by the hypothetical cold virus? The paper is a poor one, devoid of critical analysis, and the figures are not set out in any detail. From the statistical viewpoint the paper would be quite unacceptable to any research worker. This is not to say that anahist may not prove useful in relief of the common cold. But the Council on Pharmacy and Chemistry of the American Medical Association has warned against the indiscriminate use of antihistaminic drugs in treating the common cold and is not convinced that the data available are sufficient to warrant the claims made.] *M. H. Pappworth*

BACTERIAL INFECTIONS

2758. **Treatment of Leprosy with Diaminodiphenyl Sulphone by Mouth**

J. LOWE. *Lancet* [*Lancet*] **1**, 145–150, Jan. 28, 1950. 25 refs.

A review of the literature concerning the treatment of leprosy with diamino-diphenyl sulphone (DADPS) is given, and the author points out that little attempt has been made to determine either the therapeutic blood level in man, or the dosage required to maintain this level. As it appears that the more complex sulphone drugs are degraded to DADPS either in the gut or the body, the author believes that DADPS may be the active principle. If this is so a blood level of 1 mg. per 100 ml. should, on theoretical grounds, be active therapeutically. He found that, owing to good absorption from the gut and slow renal excretion, a daily oral dose of 300 mg. would maintain a level in the blood of 0·8 to 1·4 mg. per 100 ml. The drug can be detected in the blood for 14 days after stopping its administration.

A trial of DADPS in 50 cases of leprosy, mainly severe and lepromatous in type, was undertaken. The dosage was 100 mg. daily for 2 weeks, then 200 mg. daily for 2 weeks, and then 300 mg. daily. With this dosage routine toxicity tests proved unnecessary. Later, the number of patients was nearly doubled, and treatment has been given for nearly a year. In no case have the toxic symptoms of vomiting, nausea, hepatic pain, or jaundice appeared, but a slow induction is considered essential. In a few cases the dosage of DADPS has been slowly increased to 500 mg. daily without toxic effects, even after months on this regimen. All patients were given, in addition, 0·7 g. of ferrous sulphate daily.

The response in severe lepromatous cases has so far been at least equal to that obtained with "sulphetrone" or "diasone". In "tuberculoid" cases the results, even with a dosage of only 100 mg. daily, have been striking, and appear equal or superior to those obtained with other sulphones.

Febrile reactions have occurred in 30% of the lepromatous cases (as also happens with sulphetrone), treatment being temporarily suspended. Other reactions, such as neuritis, dermatitis, and eye inflammations, occur in the same proportion of cases as with sulphetrone, and anaemia has not been more common or severe. The drug is easy to give to out-patients, is relatively cheap, and periodic laboratory examinations need not be extensive. *W. H. Horner Andrews*

2759. **The Treatment of Lepromatous Leprosy with 4 : 4′-Diaminodiphenyl Sulfone in Oil. Findings in 100 Cases Treated for One Year**

B. D. MOLESWORTH, P. S. NARAYANASWAMI, and I. A. SIMPSON. *International Journal of Leprosy* [*Int. J. Leprosy*] **17**, 197–210, July–Sept., 1949. 20 figs.

A series of 100 cases of leprosy, mostly lepromatous but in some cases atypical, were treated in Malaya with 4:4′-diaminodiphenyl sulphone (DDS) for one year. A 20% suspension of the drug in purified and deodorized neutral coconut oil with 0·5% phenol was used, in an average dosage of 0·5 g. twice weekly. There was marked clinical improvement in 96 cases, and bacteriological improvement (assessed by smears from the ear lobes) occurred in 27. Improvement was evidenced by flattening of nodules and fading of colour, and by healing of ulcers. Cases complicated by pregnancy, pulmonary tuberculosis, and iritis all improved, and the results in children equalled those in adults. Levels in the blood ranged between 0·1 and 0·9 mg. per 100 ml. Complications of therapy were slight; mild secondary anaemia, lepra reactions, neuritis, and giddiness were noted, but did not necessitate cessation of treatment. Two patients had mild jaundice.

[The absence of toxic complications is surprising, and was presumably due to the low dosage employed. Details are not given of the cases in which there was slight anaemia and jaundice, and it would be interesting to know whether there was evidence of haemolysis.] *J. L. Markson*

2760. **Surgical Treatment of the Primary Lesion of Leprosy**

R. BOENJAMIN. *International Journal of Leprosy* [*Int. J. Leprosy*] **17**, 217–227, July–Sept., 1949. 19 refs.

The primary lesion of leprosy may be either a hypopigmented, anaesthetic macule or a lepromatous nodule. Treatment by surgical excision is based on the belief that by this means dissemination of the disease may be prevented. The author has excised 7 primary lesions. One was a tuberculoid papule in which bacilli were found, and 6 were macular lesions without bacilli, the diagnosis

being made on clinical grounds. A history of prolonged exposure to infection was obtained in 6 cases. None of the patients showed evidence of dissemination in the form of nerve enlargement or lymph-node swelling. Over a period of observation ranging from 3 to 12 years, no further evidence of leprosy has appeared in any of the patients from whom the primary lesion was excised.

J. L. Markson

2761. **Chloramphenicol and Other Antibiotics in the Treatment of Typhoid Fever and Typhoid Carriers**
T. E. Woodward, J. E. Smadel, and H. L. Ley. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 87–99, Jan., 1950. 6 figs., 14 refs.

This valuable paper describes the treatment with chloramphenicol of 24 patients acutely ill with typhoid fever. Some of the cases were treated in Kuala Lumpur, Malaya, and some in Baltimore, U.S.A. Diagnosis was confirmed in every case by positive blood culture. In 22 cases treatment was begun within 3 weeks of the onset of illness; the remaining 2 cases were cases of relapse at the 5th and 7th week respectively. Each patient received an initial loading dose of 3 to 4 g. (50 mg. per kg.) of chloramphenicol and throughout the febrile period 2 to 3 g. a day was given in doses of 0·25 g. every 2 or 3 hours. When the temperature had returned to normal, 0·25 g. was given every 4 to 6 hours for a further 5 days. Vomiting occurred in a few cases after the first large dose, but was avoided in later experiments by giving coated tablets; no other undesirable side-effects were observed. In every case the effects of treatment were carefully studied by repeated cultures of blood, urine, and faeces, Widal tests, blood counts, and daily estimations of antibiotic level in the blood. The average duration of fever after the initial doses was 3·5 days in primary cases and most of these patients recovered completely without complications. There were no deaths. Four patients were given less than the standard amount of drug because of shortness of supply; *Salmonella typhi* remained present in the stools, and relapses occurred 10 to 16 days after the last dose of drug. The relapses were readily controlled by further courses of treatment and there was no evidence of the development of drug resistance either clinically or in laboratory tests upon the organism. If relapse is to be avoided it appears that treatment with choramphenicol must be continued for at least 8 days.

Two patients in whom intestinal haemorrhage occurred recovered with treatment which included blood transfusions. In one case perforation took place after an ill-advised injection of pituitrin, given for the relief of gaseous distension. Treatment with intravenous fluids, blood transfusion, and massive doses of penicillin and streptomycin brought about a satisfactory recovery without surgical intervention. It is to be noted that complications are liable to occur after the temperature has returned to normal, because the patient becomes afebrile before the ulcers in the gut have healed. None of the treated patients became a chronic carrier, none had typhoid bacilli in the urine at any time, and 9 never gave a positive stool culture.

Four chronic carriers were treated for 2 weeks with large doses of chloramphenicol, 4 to 6 g. daily (with an average total dose of 71 g.). The average level of antibiotic attained in the blood was 38 μg. per ml. Duodenal drainage fluid gave negative cultures within 2 to 6 days, but cultures became positive again shortly after the end of treatment. It is suggested that the presence of the drug in the bile may have been the cause of the negative cultures during treatment, although a concentration of 1 mg. per ml. has no activity against *Salm. typhi in vitro*. In none of the carriers was the infection eradicated, although one of them also underwent cholecystectomy. The opportunity was taken in this last case to study the excretion of chloramphenicol in the bile withdrawn from a drainage tube in the common bile duct after operation. Single oral doses of 2 or 4 g. gave a level of antibiotic in the bile about half of that in the blood, and the bile-concentration curve followed the blood-concentration curve.

Four further patients were treated with aureomycin and five with polymyxin, but the course of the disease was not affected, being the same as in 9 patients to whom only supportive hospital treatment was given.

The authors draw attention to the favourable results of treatment of typhoid fever with chloramphenicol compared with the results of treatment set out in the extensive statistics available before the introduction of antibiotic therapy.

L. G. Goodwin

2762. **Experimental Study of the Therapeutic Action of Chloromycetin (Chloramphenicol) in Typhoid Fever.** (Étude expérimentale de l'activité thérapeutique de la chloromycétine (chloramphénicol) dans la fièvre typhoïde)
C. Levaditi, A. Vaisman, and J. H. Eveno. *Bulletin de L'Académie Nationale de Médecine* [*Bull. Acad. nat. Méd., Paris*] **113**, 785–795, Dec. 20, 1949. 5 figs., 25 refs.

Choramphenicol *in vitro* exerts an intense bacteriostatic action on *Salmonella typhi*, but no bactericidal action: the morphological changes induced by the antibiotic are slight. The action *in vivo* in the mouse is both bacteriostatic and bactericidal: polymorphonuclear leucocytes play little part in the disappearance of the bacilli. Resistance against chloramphenicol is not readily induced in typhoid bacilli.

G. M. Findlay

2763. **Chloramphenicol Treatment of Typhoid and Paratyphoid B in Children.** (La cloromicetina nel tifo e nel paratifo B del bambino)
L. Cartagenova, A. Ghio, F. Copello, S. Conte, and G. Vittone. *Minerva Medica* [*Minerva med., Torino*] **2**, 868–872, Dec. 8, 1949. 18 refs.

The authors treated 55 patients in Genoa with chloramphenicol. Of these, 15 had typhoid fever and 40 paratyphoid B infection. The results were uniformly favourable. The following points deserve mention.

Only children over 2 years old were given the capsules by mouth, young children receiving an aqueous solution rectally. No loading dose was given, and the authors do not consider one necessary. The maintenance dose of 50 mg. per kg. (80 to 90 mg. in infants) in typhoid and 35 to 70 mg. per kg. in paratyphoid B daily was given

in divided doses from the start. The wide variation in dosage given in the cases of paratyphoid B did not seem to affect the results. The authors emphasize that, if relapses are to be avoided, it is more important to continue administration of a moderate dose for a longer period (until at least 7 to 10 days after disappearance of fever) than to give larger doses for a shorter time. No toxic phenomena were seen, but there was in some cases of paratyphoid B a certain reduction in leucocyte count.

Occasionally a real crisis may occur during treatment with fall in temperature to much below normal, profound fall in blood pressure, and tachycardia and tachypnoea. This condition may require urgent treatment, or prophylaxis with adrenal cortical extract and circulatory stimulants.

Advantage is sometimes to be obtained in cases complicated, for example, by bronchitis from a combination of chloramphenicol and penicillin. When relapse occurs it yields rapidly to re-treatment; it would seem therefore that drug-resistance does not develop.

S. S. B. Gilder

2764. **A Clinical Study of the Treatment of Typhoid Fever with Chloramphenicol.** (Contributo clinico al trattamento del tifo addominale con cloromicetina) R. BERTO. *Minerva Medica* [*Minerva med., Torino*] **2,** 873–875, Dec. 8, 1949. 6 refs.

Brief histories are given of 5 cases of typhoid fever (one complicated by encephalitis) and 1 case of paratyphoid B treated in Verona with chloramphenicol. The author agrees with Cartagenova *et al.* that a large initial dose is unnecessary. He gave 50 mg. (2 capsules) as a first dose, followed usually by 25 mg. every 2 hours. The total dose varied from 9 to 18 g. Improvement was rapid in all cases, the first sign being cleansing of the tongue. In 4 cases the temperature fell by crisis, but no cardiovascular complications appeared.

S. S. B. Gilder

2765. **Paratyphoid B Fever Treated with Choramphenicol** M. CURTIN. *British Medical Journal* [*Brit. med. J.*] **2,** 1504–1506, Dec. 31, 1949. 3 figs., 5 refs.

Chloramphenicol was used in the treatment of 6 cases of moderately severe paratyphoid fever, 5 of which were due to *Salmonella paratyphi* B phage type 3A and one to *Salm. paratyphi* B phage type Taunton. Both organisms were sensitive *in vitro* to chloramphenicol, and in the one case in which sensitivity tests were also carried out after treatment no resistance was found to have developed. The drug was given 4-hourly, the dosage and period of administration varying. Within 24 hours of starting treatment there was a remarkable clinical improvement in all 6 cases and diarrhoea ceased in a further 2 to 8 days. In 4 cases, a convalescent carrier-state lasted for 6 to 9 weeks, but in the other 2 cases the faeces became sterile after 4 and 5 days. Three apparently healthy carriers of *Salm. paratyphi* B phage type 3A in faeces were also treated with chloramphenicol, 0·5 g. 4-hourly for 4 days and then 0·25 g. 4-hourly for 3 days. This dosage had no effect on the carrier state. *A. W. H. Foxell*

2766. **Use of Visammin in Treatment of Whooping Cough** A. KHALIL and A. SAFWAT. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79,** 42–49, Jan., 1950. 4 figs., 15 refs.

The authors report from the Kasr-el-Aini Medical Faculty, Cairo, on the effect of the antispasmodic visammin or khellin in the treatment of whooping-cough, dosage being based on that established for angina pectoris and bronchial asthma, that is, 3 to 3·5 mg. per kg. body weight for intramuscular injection.

To avoid giving injections to the children in this series the drug was used orally only, in a divided dose (3 to 4 times a day) of 4·5 to 7·5 mg. per kg. body weight. The rapid absorption and slow elimination of visammin by the body should ensure a decided and lasting bronchodilatation. The visammin content of blood samples was estimated. The preparation used was a liquid extract of *Ammi visnaga*. It was given with orange syrup and water, and no other drugs were used.

In their assessment of results the authors use a "whooping-cough index", which is the numerical product of the number of paroxysms per day, their average duration in minutes, and the average number of whoops in each. Each child was under constant observation night and day, and this index was found to be a good indication of the progress of the disease, a mild attack being associated with an index of 500 or less, and a severe one with an index over 1,000.

Of 22 children investigated 8 had a mild attack, 6 a moderate one, 6 a severe one, and 2 an extremely severe one. Each child was observed for 3 to 4 days without treatment to assess the severity of the attack. A graph of the index response shows a rapid marked decline on the first day of treatment. In one very severe case, with an index of 9,600, in an infant 40 days old, bronchopneumonia developed and penicillin was required as well, but the authors believe that visammin treatment saved this child's life. After varying the dosage and comparing responses, the authors conclude that the effective concentration of visammin in the blood is between 1 and 2 μg. per ml. *Morag L. Insley*

2767. **Pertussis Treated with Chloramphenicol** E. H. PAYNE, M. LEVY, G. M. ZAMORA, M. S. VILARROEL, and E. Z. CANELAS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141,** 1298–1299, Dec. 31, 1949. 5 refs.

In the department of Cochabamba, Bolivia, whooping-cough is a serious disease carrying a mortality of 20%, which does not appear to be related to social status. It has been found that penicillin and streptomycin prevent complications, but do not shorten the disease. *Haemophilus pertussis* and *H. parapertussis* are both sensitive to chloramphenicol *in vitro*. In this paper is described the treatment with chloramphenicol of 50 patients under 5 years of age seriously ill with whooping-cough, the diagnosis being confirmed either by cough-plate or by swab culture. The clinical history of 7 of these cases is given. The drug was given by mouth, as a rectal suppository, or intravenously, and dosage was calculated according to body weight. The therapeutic results are

reported as excellent, fever disappearing by the second day and the frequency of paroxysms decreasing considerably. The only complication seemed to be a slight nausea. Cough-plate cultures were negative after 7 days' treatment. It would appear that the drug is specific, as the authors mention neither mortality nor complications in the treated cases. *Paul B. Woolley*

2768. **Chloromycetin in the Treatment of Salmonella Enteritis**

S. Ross, F. G. Burke, E. C. Rice, J. A. Washington, and S. Stevens. *New England Journal of Medicine* [*New Engl. J. Med.*] **242**, 173–176, Feb. 2, 1950. 4 refs.

Nine cases of salmonella enteritis in infants were treated with "chloromycetin". The chloromycetin sensitivities of the various strains of salmonella isolated from these patients ranged from 2 to 5 μg. per ml.

In spite of the ready susceptibility of the organism to the drug, only 2 of the 9 patients in this series became permanently free of the pathogen after treatment. In the other 7 cases a transitory inhibitory effect on both the salmonella organism and the normal stool flora was observed; however, within 5 to 40 days after chloromycetin was discontinued the pathogen reappeared in the stools. No increase in chloromycetin resistance was observed in any case after bacteriologic relapse.—[Authors' summary.]

2769. **The Effect of Polymyxin in the Treatment of Experimental Brucellosis and Tularemia**

C. L. Larson, B. N. Carle, and A. E. Verder. *Annals of the New York Academy of Sciences* [*Ann. N.Y. Acad. Sci.*] **51**, 982–986, 1949. 5 refs.

Experiments were undertaken to study the effect of polymyxin on brucellosis and tularaemia in animals. In the first experiment 24 guinea-pigs weighing about 350 g. were divided into 2 groups, one of which was infected intraperitoneally with 12 and the other with 12,000 *Brucella suis* organisms. In each group of 12 animals 6 were left untreated, 3 were treated with a single daily subcutaneous injection of 6·4 mg. per kg. body weight of a polymyxin preparation containing 1,000 units per mg., and 3 were given a similar injection twice daily. Treatment was started 19 to 20 days after infection and continued for 9 to 10 days. The animals were killed one day later and agglutination tests and cultures made, including a quantitative culture from a weighed portion of the spleen. No differences were apparent in the number of organisms thus isolated as between treated and untreated animals.

In a second experiment 25 guinea-pigs were infected intraperitoneally with 3,400 *Br. suis* organisms. Treatment of the survivors with a second preparation of polymyxin, containing 900 to 950 units per mg., was started 24 days later; 8 animals were given 1·5 mg. every 4 hours for 10 days, 6 were given 1·25 mg. of polymyxin and 2·5 mg. of streptomycin every 4 hours for 10 days, and 11 were left untreated. No differences were apparent in the degree of infection as between the three groups. In a third experiment 42 guinea-pigs were injected subcutaneously with 950 *Br. suis* organisms and 14 days later treatment of the survivors was started, 11 being given a third preparation of polymyxin containing 6,000 units per mg., 5 mg. per kg. daily in 6 subcutaneous doses for 14 days; 12 were treated for the same length of time with sulphadiazine, 100 mg. per kg. once a day orally, and streptomycin, 30,000 units per kg. daily in 6 subcutaneous doses; while 14 were untreated. At necropsy it was again found that polymyxin had had no effect on the course of infection, whereas only 2 of the animals treated with sulphadiazine and streptomycin yielded positive cultures.

Finally, a group of 37 mice were infected intraperitoneally with 60 to 100 MLD of *Pasteurella tularensis*. Twenty-four hours later 17 were treated with the preparation of polymyxin used in the second experiment, 0·125 mg. being given twice a day. All treated and control animals were dead 120 hours after infection. *Mary Barber*

2770. **Treatment of Chronic Brucellosis with Chloramphenicol and Aureomycin**

R. J. Ralston and E. H. Payne. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **142**, 159–161, Jan. 21, 1950. 11 refs.

In 45 cases a diagnosis of chronic brucellosis was made upon the following grounds: (1) a history of contact with infected animals or their products; (2) vague chronic illness with fatigue, weakness, aches, sweats, nervousness, and low-grade fever; (3) a normal or low leucocyte count; (4) a low erythrocyte sedimentation rate; and in some cases (5) a positive agglutination or skin reaction or a history of improvement when injections of *Brucella* antigen were given.

Four patients were treated with 2·5 to 3·5 g. of aureomycin hydrochloride daily for 10 days. Prompt relief was obtained in 2 cases and partial improvement in one; the remaining patient was unable to complete the course because of the severe side-effects—diarrhoea and vomiting. The other patients were treated with 18 to 27 g. of chloramphenicol by mouth, given in 7 to 12 days. Children were given a total of 9 g. Complete or partial improvement occurred in 35 patients, and during an observation period of 3 to 8 months there were only 3 relapses. It is thought that some of the failures may have been due to errors of diagnosis, which is very difficult in the chronic phase of this infection. Side-effects of treatment with chloramphenicol were slight. In an addendum similar results in a further 22 patients are reported. *L. G. Goodwin*

2771. **Aureomycin Therapy in Human Brucellosis Due to *Brucella abortus***

A. I. Braude, W. H. Hall, and W. W. Spink. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 831–835, Nov. 19, 1949. 8 refs.

The authors have already reported good results with aureomycin in the treatment of *Brucella melitensis* infections, and now report rapid and striking clinical improvement in 16 consecutive cases in which *Br. abortus* was isolated by culture from the blood. About one-half of these were acute infections (less than

2 months' duration) and the rest chronic (over 4 months' duration). The patients' ages ranged from 18 months to 60 years. Six of the cases were complicated by other diseases or by unusual manifestations of the *Brucella* infection. Response to therapy was generally as satisfactory in patients with complications as in the uncomplicated cases. With 3 exceptions all treated persons had become afebrile by the end of the 4th day, and the longest period of fever after the start of the treatment was 7 days. The subjective symptoms and severe drenching sweats of the disease also subsided promptly.

The dosage for adults and older children was 2 g. daily in 4 doses at 6-hourly intervals over a period of 10 to 16 days. Infants and small children received 0·6 to 1 g. daily. The 16 patients were observed for about 2 to 7 months, during which time one bacteriological relapse and two possible clinical relapses (or intercurrent infections) occurred. In these a second course of aureomycin apparently eliminated the infection. The drug was well tolerated. Possible side-effects—epigastric pain and nausea—were experienced by 5 patients, but there was not sufficient distress to make reduction of the dosage necessary.

The authors consider that aureomycin is effective against both *Br. melitensis* and *Br. abortus* infections, and is to be preferred to combined streptomycin and sulphadiazine treatment owing to the absence of serious side-effects. In the routine treatment of these infections little is to be gained by the additional use of dihydrostreptomycin.

H. Stanley Banks

2772. **Oral Administration of Killed *Brucella* to Man**
N. B. McCULLOUGH, C. W. EISELE, and G. A. BEAL. *Public Health Reports, Washington* [*Publ. Hlth Rep., Wash.*] **64**, 1613–1616, Dec. 16, 1949. 2 refs.

This investigation was carried out to determine whether the ingestion of dead *Brucellae* in dairy products might be responsible in human beings for the presence of antibodies. Large amounts were given, one group of 10 men swallowing a thousand million bacterial cells on 49 occasions over a period of 6 months. In the first series the selected men were chosen from those who showed no antibodies in the serum or any other evidence of reaction to *Brucellae*, and no evidence was obtained of altered reaction after ingestion of the bacterial cells.

Another group of 12 men who showed some evidence of previous contact with *Brucella* (antibodies or positive skin reaction) were similarly treated, and in 6 there was some slight evidence of increase in antibody titre.

Scott Thomson

2773. **A Study of Three Cases of Tularaemia Occurring in the Paris Area.** (Étude de trois cas de tularémie observés dans la région parisienne)
P. DELAFONTAINE, G. DAMIENS, and P. GARNIER. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **25**, 4027–4030, Dec. 30, 1949. 1 fig.

The authors report 3 cases of tularaemia observed at the Hôpital de Saint-Denis, Paris. The patients were all members of one family and were infected by eating the uncooked meat of a rabbit which had been purchased in a local street market, this being the first occasion in which such an infection has been traced to a rabbit in France. The clinical manifestations in these cases, which are described in detail, show how polymorphic the disease can be. In the first case (a girl of 12) the classical ulcerative-bubonic form was observed; in the second, lymph-node and ocular lesions predominated; in the third (a boy aged 5) the disease ran a subclinical course, the diagnosis being reached by laboratory methods. Inoculation of pus from local abscesses into guinea-pigs permitted the isolation of the first pure strain of *Pasteurella tularense* ever recovered in France. The authors consider that streptomycin (1 g. daily for 10 days) was undoubtedly of value in treatment, especially in the first case, which came under observation at an early stage, but consider that other antibiotics such as aureomycin may prove to be more effective, since virulent organisms could still be obtained from the pus after 4 days' treatment with streptomycin.

Jos. B. Ellison

TUBERCULOSIS

2774. **The Subsequent Course, under Sanatorium Treatment, in Cases of Tuberculosis Detected by Routine Radiological Examination.** (Le devenir en milieu sanatorial des tuberculoses décelées par le dépistage radiologique systématique)
—. AUDOYE, —. CONSTANS, —. MANQUÈNE, and —. PILON. *Revue de la Tuberculose* [*Rev. Tuberc., Paris*] **13**, 934–940, 1949. 2 figs.

During the three years before March, 1949, 565 young men suffering from pulmonary tuberculosis were admitted to a sanatorium. In 140 of these the disease had been discovered by periodic radiographic examination. In the remaining 425 the condition was diagnosed after symptoms had arisen. In the former group the first examination revealed pulmonary cavities in 47, solitary round shadows in 6, and miliary tuberculosis in 3. By the time the patients were admitted to the sanatorium the number of those with radiographic evidence of cavitation had risen to 59. In 75 of the 140 the diagnosis was confirmed by the first sputum examination. In the remaining 65 tubercle bacilli were not detected until after repeated sputum examinations or guinea-pig inoculation. This caused up to several months' delay in admission to the sanatorium. The delay is thought to have led to the rise in the number of lesions with cavitation and an increase in the period of sanatorium treatment, this period being directly proportional to the time elapsed between diagnosis and admission. It is claimed that the group in which there was the least delay in confirmation of diagnosis, and consequently in starting treatment, did better during their stay in sanatorium. [The differences are too small to support this conclusion.]

It is suggested that prolonged search for tubercle bacilli, which is done more for administrative than medical reasons, may nullify the advantages that come from early diagnosis by periodic chest radiography. Among those cases not diagnosed until symptoms had

appeared there was a higher percentage of cases requiring surgical collapse treatment or streptomycin, and in this group a longer period of institutional treatment was also needed; 18% remained in the sanatorium for 12 months compared with only 0·15% of the patients whose condition was discovered by routine radiography.

J. R. Bignall

2775. **Topical Detergent Antibiotics in the Treatment of Tuberculous Sinuses**

E. J. Grace and V. Bryson. *Diseases of the Chest* [*Dis. Chest*] **16**, 795–800, Dec., 1949. 3 figs., 5 refs.

Streptomycin was the first really effective weapon in the treatment of the chronic draining tuberculous sinus. It has mainly been used in the usual 1- to 3-g. daily doses given intramuscularly. The authors, however, argue that for the sinus alone this is unnecessary as everything depends on the concentration of the drug at the site. They therefore used two antibiotics, streptomycin and penicillin, combined with a detergent germicide to reduce surface tension, and injected the solution directly into the sinus tract. The solution was prepared by dissolving 1 million units of penicillin and 1 million units of streptomycin in 100 ml. of 1 in 1,000 aqueous solution of " zephiran chloride ", and 4 ml. was instilled 8-hourly night and day. A case is described of chronic tuberculous empyema in which a discharging sinus developed in the left axilla. After this had been present for 7 years it was closed by use of topical streptomycin and a germicidal detergent. It healed for 17 months but broke down again in a different site. On the second occasion the solution described above was used and after 8 days the sinus promptly closed. It has remained closed for 15 months so far.

The authors believe that zephiran, a quaternary ammonium germicide, potentiates the action of penicillin though not of streptomycin. By reducing the surface tension it enhances penetration. Altogether they recommend this method as being simple, rapid, cheap, and safe, and achieving as good a result as parenteral administration of streptomycin. *Ronald S. McNeill*

2776. **Acute Infiltration of the Pulmonary Hilum.** (Gli infiltrati dell'ilo polmonare a decorso acuto)

A. M. Michelazzi. *Omnia Medica* [*Omnia med.*] **27**, 381–429, July–Dec., 1949. 7 figs., 17 refs.

A series of 74 cases of an acute febrile illness, characterized by hilar adenitis and a surrounding pneumonic reaction, is described in patients who attended the Institute of Clinical Medicine and Therapeutics of the University of Pisa.

The incidence was highest in the spring of 1943 and 1944, and in the age groups 16 to 25, there being no discrimination between the sexes. In 31 cases there was a family history of tuberculosis and 24 had had some form of upper respiratory infection shortly before.

The onset was sudden with a high intermittent or remittent fever, pains in the muscles and joints, headache, sweating, mild sore throat, and a cough with a little mucous sputum. Physical signs in the chest were of little diagnostic value, but were present sometimes in the interscapular region. Air entry might be diminished with increase of vocal resonance and fremitus and occasional coarse crepitant rales. Movement was diminished at the base on the affected side. In the majority both spleen and liver were palpable one to two fingerbreadths below the costal margin, and in 12 cases there was enlargement of the cervical and submandibular lymph nodes. The fever always resolved in 3 to 4 weeks, the differential diagnosis in early stages being from influenza, typhus, brucellosis, Loeffler's syndrome, miliary tuberculosis, and malaria.

All serological reactions, blood films, and sternal marrow were normal. The erythrocyte sedimentation rate, however, was invariably raised to about 30 mm. in one hour whilst the fever lasted, and the Mantoux reaction was strongly positive. In some patients there was a transient albuminuria.

The radiological changes did not appear at the onset, but in common with the splenomegaly persisted for some months. In all cases there was a hilar enlargement with a characteristic surrounding pulmonary infiltration above or below the hilum, with ill-defined edges. Right and left sides were equally affected, but in one case only were bilateral changes seen. No signs of active tuberculosis were observed, but in nearly half the cases there was evidence of a healed primary lesion. Pleural effusion later developed in 2 cases.

Treatment was empirical. Amidopyrine was given, except in 4 cases in which streptomycin 0·5 g. was injected intramuscularly once a day, for 40 days.

The underlying nature of the disease is discussed at great length, and the author concludes that it is a tuberculous reaction of hypersensitivity, initiated by some intercurrent infection. An analogy is drawn with erythema nodosum and primary tuberculous effusion.

Donough O'Brien

2777. **The Use of Dihydrostreptomycin in the Treatment of Tuberculosis**

D. T. Carr, H. C. Hinshaw, K. H. Pfuetze, and H. A. Brown. *Diseases of the Chest* [*Dis. Chest.*] **16**, 801–821, Dec., 1949. 2 figs., 14 refs.

The search for a drug with the same activity as streptomycin in tuberculosis, but with less neurotoxicity as measured by vestibular damage, prompted this study of dihydrostreptomycin. Dihydrostreptomycin is prepared by catalytic hydrogenation of streptomycin and has the same inhibitory effect on tubercle bacilli *in vitro*. Unfortunately streptomycin-resistant strains are equally resistant to dihydrostreptomycin. Experimental studies on animals, however, show that the latter drug causes much less vestibular damage and that this is not due to differences in concentration in the various body fluids.

In this study both the hydrochloride and sulphate of dihydrostreptomycin were used and the dose was 1 g. intramuscularly, given at intervals of 8 to 12 and 24 hours. Tests of vestibular function (by the method of Kobrak) were performed on all patients before, during, and after treatment, and complaints of dizziness, deafness, visual disturbances, and paraesthesiae noted.

Of 35 patients treated, 26 received 2 g. per day over long periods (usually 60 days) and of these only 4 showed

signs or symptoms of vestibular damage. These 4 were receiving more than 30 mg. per kg. body weight, and the remaining 22 less than 30 mg. per kg. Two patients noted slight deafness and audiograms revealed high-frequency deafness in one case.

Other toxic manifestations such as allergic signs, liver and kidney damage, blood dyscrasias, and local irritation were looked for. No allergic reactions occurred, though the blood of 9 of the 35 contained 7·5% or more of eosinophils. Local irritation at the site of injections decreased as the preparations used became purer. No other toxic signs appeared. The authors considered dihydrostreptomycin to be as therapeutically effective as streptomycin in various types of tuberculosis, but state that more work is necessary to decide whether they are equally effective in equal doses.

The frequency of production of resistant strains is not yet known, but in 3 patients resistant strains appeared during treatment—in 1 after only 18 days. The major problem of resistant strains therefore remains.

Ronald S. McNeill

2778. **Miliary Tuberculosis Caused by Intravenous Self-injection of Tubercle Bacilli, Treated Successfully with Streptomycin Therapy**

O. R. Jones, W. D. Platt, and L. A. Amill. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **60**, 514–519, Oct., 1949. 8 figs., 1 ref.

A woman bacteriologist, aged 27, accidentally punctured the skin of her antecubital fossa with a needle contaminated with tubercle bacilli. A very small superficial papule appeared at the puncture site and disappeared after a few weeks. A year later a tuberculin test was positive. Three years after this accidental infection, she injected herself intravenously with 1 ml. of a suspension of virulent strain of tubercle bacilli with possible suicidal intent. She was admitted to hospital the following day, complaining of loss of weight, night sweats, fatigue, urinary frequency, " pus in her urine ", and a chronic non-productive cough of 3 months' duration, but she did not reveal her self-inoculation. Her temperature was raised on admission but fell to normal the following day and remained normal during the 8 days she was under observation in hospital. Blood count, urine examination, erythrocyte sedimentation rate (E.S.R.), and chest radiography revealed no abnormality. Cystoscopy revealed signs of a subsiding infection of the bladder, but there was no evidence of tuberculous infection and a guinea-pig inoculation test was negative. She subsequently stated that she had noted swelling, redness, and tenderness in the elbow and had squeezed a small amount of pus from the lesion and found tubercle bacilli in the smear.

On the day after discharge from hospital she began to have severe rigors and fever and was readmitted to hospital on the 15th day after the intravenous inoculation. Results of clinical and laboratory examinations were still negative, except for an E.S.R. of 56 mm. in one hour. As there was considerable scepticism about the history of self-inoculation, treatment was delayed for another 6 days. Streptomycin (3 g. daily intramuscularly) administration was then begun as a result of the appearance of generalized miliary infiltration of the lungs 21 days after the inoculation. At this time tubercle bacilli were cultivated from a small amount of serum expressed from the site of inoculation, but blood cultures and guinea-pig tests of blood, urine, and cerebrospinal fluid were all negative. The leucocyte counts remained within normal limits, but a mild hypochromic microcytic anaemia necessitated one blood transfusion and iron administration. The tuberculin reaction was positive. Pyrexia continued. Fortunately the strain of tubercle bacillus cultivated from the antecubital fossa was streptomycin-sensitive. On the 23rd day of streptomycin therapy a dramatic improvement began. Three days later the temperature became normal, the miliary lung lesions began to clear, the lesion in the antecubital fossa healed, and she was discharged from hospital 125 days after admission. Altogether she had received 241 g. streptomycin over a period of 105 days.

A follow-up inquiry elicited the information that she had remained well and had married. The authors quote from French literature a similar case in a male aged 29. In this instance streptomycin was not available and the patient became progressively worse and died of tuberculous meningitis at the end of 3 months.

S. Roodhouse Gloyne

2779. **Streptomycin in the Treatment of Miliary and Meningeal Tuberculosis. Based on a Study of 30 Cases**

A. Shamaskin, E. J. Des Autels, H. C. Sweany, L. C. Morris, J. R. Zvetina, and J. Mindlin. *Diseases of the Chest* [*Dis. Chest*] **16**, 765–789, Dec., 1949.

2780. **Streptomycin in the Treatment of Tuberculosis in Children**

E. M. Jones and W. L. Howard. *Diseases of the Chest* [*Dis. Chest*] **16**, 744–760, Dec., 1949. 8 refs.

At Maybury Sanatorium, Michigan, 101 children, from April, 1947, to January, 1949, were treated with streptomycin and the results are compared with those in control cases from a previous period. Five groups of cases were treated: (*a*) cases of miliary and meningeal tuberculosis; (*b*) cases of severe primary pulmonary tuberculosis; (*c*) cases of primary disease with bronchial complications; (*d*) cases of reinfection; and (*e*) cases of extrapulmonary tuberculosis.

In group (*a*) 55 to 88 mg. per kg. body weight per day was given for 3 to 6 months and 25 to 44 mg. for the balance of the 6 months. The daily total was divided into 2 or 3 doses. When meningitis was present 2·5 mg. per kg. up to a maximum of 50 mg. was given intrathecally daily for 3 weeks, then 3 times per week for 3 months and half that dose twice weekly for the balance of 6 months. Eighteen cases of miliary tuberculosis, 9 of meningitis, and 4 of miliary tuberculosis with meningitis were so treated. One patient with miliary meningitis died in relapse but the rest all recovered and were well in May, 1949. All had vestibular damage but this was well compensated. One is deaf. Without streptomycin 100% of patients with meningitis and 80% with miliary disease had died.

In group (*b*) 33 to 66 mg. per kg. was given for 4 to 7 days, then half the dose 3 times per week for a total

of 42 doses. Of 5 babies treated 3 recovered and 2 are progressing well.

In group (*c*), which includes cases of epituberculosis, 35 children were treated. They received 15 to 33 mg. per kg. for 4 to 7 days and 15 to 22 mg. 3 times per week for a total of 42 doses. All survived and apparently recovered. None suffered vestibular damage. Of the previously treated controls 15% had died in 2 years and 28% in 10 years. This represents a marked improvement, and the prevention of spread to other parts of the body was particularly noteworthy. The future incidence of bronchiectasis is expected to be markedly reduced.

In group (*d*) 5 children, from 5 to 11 years of age, were treated with the same dosage as group (*c*). All survived and 4 are expected to recover. Four out of 9 died within 2 years in the control group. In group (*e*) are included 13 cases of bone and joint tuberculosis, 2 of adenitis with sinus formation, 2 of pleuritis, 2 of peritonitis, 1 of pericarditis, and 1 of renal disease. Local therapy was given together with streptomycin, the latter being administered in the same doses as in group (*c*) but as many as 84 doses being given if necessary. After aspiration 22 mg. was instilled into the pleural space. In all 21 children the condition improved.

The over-all picture shows a reduction in death rate from 15 to 1% for comparable 26-month periods when streptomycin is used. [This is impressive and the authors' findings and discussion are well worth studying.]

Ronald S. McNeill

2781. **Treatment of Tuberculous Meningitis with Streptomycin**

S. J. M. Russell and P. MacArthur. *Lancet* [*Lancet*] **1**, 59–63, Jan. 14, 1950. 2 figs., 17 refs.

Observations were made on 33 cases of tuberculous meningitis treated with streptomycin at the Royal Hospital for Sick Children, Glasgow, over a period of 2½ years. After some early variation, the intramuscular dosage of streptomycin was standardized at 20 mg. per lb. (44·5 mg. per kg.) body weight daily, given 12-hourly. The blood streptomycin level reached its peak (average 80 μg. per ml.) after 1 hour and fell gradually over the next 12 hours to 1 to 16 μg. per ml. A concentration in the cerebrospinal fluid of 8 μg. per ml. was commonly found, during the active stage of meningitis, 1 to 4 hours after intramuscular injection, and 1 μg. per ml. was often detectable 24 hours later. For intrathecal injection a dose of 50 mg. for children over 3 years of age, and 25 mg. for those below that age, in a volume of 5 to 10 ml. was found adequate. Two schedules of treatment were evolved, one consisting of a course of 12 weeks' continuous intramuscular treatment, and the other of 3 or 4 separate courses of 4 weeks at 2-week intervals. Both included intensive intrathecal treatment at the beginning with some subsequent intermittent injections.

The 33 cases are recorded in detail. There were 18 deaths, and of the survivors 10 are reported to be well and 5 disabled. After a period of observation varying from 12 to 32 months, the general conclusion reached is that " when treatment is started early and there are no complicating factors most of the patients recover ".

Malcolm Woodbine

2782. **Factors Influencing the Outcome of Streptomycin Therapy of Pulmonary Tuberculosis**

W. B. Tucker. *Diseases of the Chest* [*Dis. Chest*] **16**, 714–743, Dec., 1949. 3 figs., 12 refs.

The author has made an extremely careful analytical study of results supplied by Veterans Administration, Army and Navy, and the Minneapolis Veterans Administration Hospital. [Only those specially interested will have the time and inclination to follow him step by step but the conclusions he reaches on the factors influencing streptomycin treatment in pulmonary tuberculosis are important.] The Veterans Administration study shows that a dose of 1 g. per day is therapeutically effective and rarely produces serious toxic manifestations. Courses lasting for 42 and 60 days, while not quite as effective as a longer course, are preferable because of the definitely lower incidence of streptomycin-resistant tubercle bacilli. The study also suggests that results are better if streptomycin administration is combined with collapse therapy when the disease is progressive before streptomycin is given, and when the disease is moderately advanced as opposed to minimal and far-advanced disease.

At the Minneapolis Veterans Administration Hospital 86 cases were studied, 57 treated according to a strict schedule for pulmonary tuberculosis, and 29 of less extensive pulmonary disease treated primarily for extrapulmonary tuberculosis. All cases had an acute or subacute component: in some there was also a chronic component. In this " mixed " group the outcome of therapy was inferior to that in the more acute and subacute cases. Results were definitely superior when collapse therapy was used at the period of maximum benefit from streptomycin. This was especially true of the " mixed " cases.

Radiographic evaluation alone is inadequate unless the degree of improvement is capable of standard assessment, particularly in the early months of treatment. Sputum conversion and relapse rates, and later on mortality rates, are important additional criteria. It is concluded that the response of cavities to streptomycin and any added treatment remains the most important factor in reaching a reliable prognosis. If the cavity formation can be controlled promptly streptomycin may yield still better results in the treatment of pulmonary tuberculosis.

Ronald S. McNeill

2783. **Treatment of Pulmonary Tuberculosis with TB I/698 (Preliminary Results).** (Die Behandlung der Lungentuberkulose mit Tb I 698 (vorläufige Mitteilung))

A. Koepchen. *Deutsche Medizinische Rundschau* [*Dtsch. med. Rdsch.*] **41**, 1149–1154, Dec. 3, 1949.

The present author records his experience with the new drug " TB I/698 " (thiosemicarbazone) in the treatment of pulmonary tuberculosis, and of its effect on non-pulmonary lesions. Toxic side-effects, such as anaemia, leucopenia and agranulocytosis, parenchymal liver and kidney damage, skin eruptions, and conjunctivitis, can be avoided if the dosage in adults does not exceed 0·1 g. (2 tablets) a day. It is advisable to start with one tablet (0·05 g.) per day, to increase the dose after a few days to

0·1 g., and to stop the medication as soon as toxic reactions such as erythemia or urticaria, urobilinuria, or leucopenia are noticed. Slight albuminuria without casts or cells is harmless. TB I/698 does not cure the disease. In the presence of cavities collapse therapy will usually be necessary. The best results are seen in cases of acute spread and in exudative lesions. Old chronic, fibrotic lesions are unsuitable for this treatment. Some striking results have been seen in ulcerations of the mucous membranes (mouth, larynx, intestine) even where the lung disease was relentlessly progressing. Gottel found the drug successful in about 30% of 175 cases; The author, who treated 50 cases, found 9 materially improved and 10 slightly improved; in 22 the condition remained stationary and in 9 there was complete failure. The great psychological advantage of offering patients previously untreated some active treatment is stressed. So is the need for watching closely blood count and urine in order not to miss the onset of toxic effects on blood, liver, or kidneys.

[No mention is made of drug resistance towards TB I/698. The results reported here do not materially differ from those previously published. One does not gain the impression that the new drug is in any way superior to either streptomycin or *para*-aminosalicylic acid, though it might be useful as an alternative.]

E. G. W. Hoffstaedt

2784. **A Preliminary Report on the Use of *para*-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis**
H. C. Sweany, G. C. Turner, M. Lichtenstein, and S. Entin. *Diseases of the Chest* [*Dis. Chest*] **16**, 633–660, Dec., 1949. 21 figs.

The objects of this study were to determine: (*a*) the toxicity of *para*-aminosalicylic acid (PAS) in human subjects; (*b*) its effect on clinical tuberculosis; (*c*) whether it decreased the development of resistance of tubercle bacilli to streptomycin; (*d*) whether it would give successful results to any extent after streptomycin treatment had failed.

The best method of administration was by giving a liquid preparation of 3 g. of the salt of PAS and $NaHCO_3$ orally, 4 times daily with food. Complete blood counts, biochemical analysis, urine analysis, blood level assays of PAS, tests of sensitivity of organisms to PAS, and radiographic analysis by unbiased observers were carried out in all cases. The cases were of 2 general types—acute exudative, and chronic fibro-caseous and ulcerative lesions. Almost all were far advanced, and so far as possible they were matched with controls. In all, 40 cases received PAS. Six were of the acute exudative type, 18 of the chronic fibro-caseous and ulcerative type (further divided into groups of 5, 8, and 5 according to the length of treatment—120, 90, and 60 days), 9 were of mixed type and were cases in which streptomycin treatment had failed, and 7 were of mixed type in which streptomycin and PAS were used together. Among cases treated with PAS alone there was a rather uniform improvement in 50 to 60% of the acute and chronic cases. The majority of the chronic fibro-ulcerative cases were, however, not benefited. The degree of improvement was greater than in the control cases, but improvement was probably a little less and slower than in corresponding cases treated with streptomycin; treatment can, however, often be continued much longer than with the latter. Where streptomycin treatment had failed administration of PAS improved 55% of cases, and in 44% the improvement was marked. In some of these cases the prognosis was hopeless and therefore the success of PAS treatment was most encouraging.

Where PAS was used with streptomycin all cases were improved but the group was small. Similarly a final opinion on delayed resistance to streptomycin could not be given. PAS appeared free from permanent toxic action. Nearly always it produced nausea in the early days. Apart from 1 case in which albuminuria was aggravated and a few cases of skin reaction all other toxic effects were gastro-intestinal. The measures for combating this are discussed. The effect of PAS on cough, sputum, weight, and fever was almost always favourable. Only in 3 cases (roughly 10%) did bacilli resistant to PAS develop; this is in marked contradistinction to streptomycin.

The authors conclude that PAS has a definite field of usefulness in the treatment of pulmonary tuberculosis.

Ronald S. McNeill

2785. **PAS in Pulmonary Tuberculosis**
G. Vallentin, E. Törnell, A. Beskow, B. Carstensen, R. Thune, G. Helleberg, and J. Lehmann. *Tubercle* [*Tubercle, Lond.*] **31**, 2–10, Jan., 1950. 6 figs., 12 refs.

This is the report of an investigation organized by the Swedish Association for the Prevention of Tuberculosis at six sanatoria, the laboratory work being carried out by Lehmann. A list of rules for selection of cases for treatment with *para*-aminosalicylic acid (PAS) was laid down, the most important being that there should be a preliminary observation period of at least 2 months and a follow-up period of 3 months, and that exudative as well as proliferative factors should be present; collapse therapy, though it might already be proceeding, was not initiated during the course. In all, 378 cases were treated, but only 205 (the "selected" group) fulfilled the criteria and these included "a number of old hopeless cases with cavities". Intestinal tuberculosis complicated 24%, tracheo-bronchial lesions 15%, and empyema 10·7% of the selected group. In 40% collapse therapy was still being continued.

The duration of the course varied from one to more than 6 months. The PAS was given as enteric-coated granules in an average daily amount of 14 g., divided into 4 to 6 doses. Intestinal symptoms when they occurred were countered by giving magnesium oxide or drops of tinct. opii before PAS, the latter being given after a meal with milk, butter, and bread.

Under the conditions of the trial, accurate assessment was difficult, but certain effects were obvious. In the majority of cases temperature fell, erythrocyte sedimentation rate fell, and weight was gained because appetite increased. There was "considerable regression" in radiological appearances in 35·6% of the selected group, whilst cavities "closed or were lost to view" in 18·3%. Improvement continued in 57% during the subsequent observation period.

The conclusion reached is that " PAS treatment has been found able to change the normal picture of the clinical events in cases of pulmonary tuberculosis in converting a progressive phase into a healing phase ".

J. V. Hurford

2786. **Treatment of Tuberculosis with Promizole. A Clinical Investigation with Matched Controls**

H. A. BURNS, W. H. FELDMAN, H. C. HINSHAW, J. A. MYERS, and K. H. PFUETZE. *Diseases of the Chest* [*Dis. Chest*] **16**, 867–869, Dec., 1949.

The therapeutic efficacy of 4: 2-diaminophenyl-5-thiazolesulphone or " promizole " was tested by a clinical investigation, with matched controls, of cases of tuberculosis in the mental hospitals in Minnesota. Serial radiographs over a period of years were available in these cases; in those selected for the study disease was progressive and in general exudative and bronchopneumonic in type. Any with lesions of a chronic nature were excluded. Patients were paired so that age and disease were as closely comparable as possible. A coin was then tossed to decide which should be the control and which should receive the promizole. Difficulties because of psychiatric conditions were considerable. Some refused oral medication and in others toxic reactions occurred. Because of this quite a number had to be excluded. Clinical records were adequate and radiographs were taken monthly. Results were evaluated on radiological improvement alone. Films were assessed by observers with no knowledge of the treatment.

The study started in the autumn of 1943 and ended in December, 1944. Only 24 pairs (48 patients) eventually qualified for assessment of the trial. Of all patients 66% were dead or worse and only 15% had shown any improvement, and that was usually slight. There was little difference in the treated and control series. It is possible that the conditions of the trial were too strict and that patients with mental disease respond poorly to treatment, but the authors feel that temporary improvement at any rate would have been observed had streptomycin been available then.

Ronald S. McNeill

2787. **Immediate Sequelae of Extrapleural Pneumothorax.** (A propos des suites immédiates du pneumothorax extrapleural)

P. RAZEMON. *Acta Tuberculosea Belgica* [*Acta tuberc. belg.*] **40**, 3–7, Dec., 1949. 1 fig.

The author reviews the most important post-operative complications of extrapleural pneumothorax in 160 recent cases of his own. The incidence of infection has become negligible since the introduction of antibiotics. Haemorrhage was unpredictable, and not related to the difficulty of the operation. Rigid haemostasis with diathermy and packs was not considered absolutely essential; but when large clots did form, good results were obtained by reopening and clearing out the cavity. In 4 cases there was severe shock starting 24 to 48 hours after operation with low blood pressure, rapid pulse, pallor, and some dyspnoea. In each case a blood-stained serous effusion was found. Two of these patients died, and it is suggested that compression of the auricles might have been the cause.

Of the less serious complications, effusions were common, but after several aspirations the cavities became dry in about 3 weeks. Surgical emphysema occurred especially where the pleural stripping had been difficult, appearing not around the incision, but in the anterior triangle of the neck and in the subclavicular and substernal areas. In an attempt to reduce the incidence of effusion and surgical emphysema the walls of the cavity were painted with citrated human plasma after haemostasis had been secured at operation. Any excess of plasma was removed, and the procedure then repeated with a thrombin solution, again mopping out excess [*cf.* the use of calcium alginate gel by Millard (*Thorax*, 1948, **5**, 233)]. This method was found to be most successful. When muscle fragments were similarly treated *in vitro* the fibrin not only coated the surface, but also infiltrated between the superficial fibres.

[No actual figures of the incidence of effusion and surgical emphysema are given, nor is mention made of other complications that may arise, such as rupture of cavities, mediastinal shift, and post-operative pain and fever.]

Donough O'Brien

2788. **Report on 140 Cases of Extrapleural Pneumothorax.** (Rapport sur 140 cas de pneumothorax extrapleuraux)

R. PANNIER. *Acta Tuberculosea Belgica* [*Acta tuberc. belg.*] **40**, 8–23, Dec., 1949.

The author gives an account of the results of extrapleural pneumothorax in the treatment of 142 cases of pulmonary tuberculosis over a 2-year period at the Hospital of Saint John, Bruges. The technique was orthodox, but is only very briefly described. In 80 cases high spinal analgesia with 1 in 1,500 cinchocaine was used, and its advantages in providing a bloodless field, easy separation of the pleura, and maintenance of the cough reflex are stressed. In 2 cases the operation had to be abandoned, and in 2 others rupture of a cavity necessitated a lobectomy. The remaining patients were divided into four groups: (1) those with cavities in the upper zone about 3 cm. in diameter or less, and with little surrounding infiltration (60 cases); (2) those with more advanced ulcero-fibrotic lesions of the apices (57 cases); (3) those in whom intrapleural pneumothorax had failed (15 cases); and (4) those cases in which bilateral extrapleural pneumothorax was required (6 cases). The operative and post-operative complications and the end results are described, and are analysed in detail in five tables.

Rupture of the cavity was the most serious complication at operation, occurring in 5 cases. Post-operative complications included effusion in 50% of cases, fever in 14%, haemorrhage and " epituberculosis " in 5%, and infection, fistulae, and collapse rarely. The early causes of death were cardiac failure in 5 cases, contralateral spread in 4, and haemorrhage and empyema in one case each; the late causes were empyema in 6 cases, effusion on the other side in 2, and spread of disease in the lung or elsewhere in 3. Bilateral disease was present in 46% of the patients, and of these 30% were thought to be cured, the rate of cure being 60% in the remainder.

A comparison was made between the results obtained in group (2) with those obtained with thoracoplasty in 66 similar cases. With the latter procedure the prognosis was twice as good. The conclusion is reached that extrapleural pneumothorax is of sound value in cases of medium-sized upper-zone cavities where intrapleural pneumothorax has failed and where it is desirable to avoid the deformity of thoracoplasty.

[No emphasis is laid on the value of this operation in bilateral disease and as a preliminary to thoracoplasty, as shown by many surgeons in Great Britain (see Reid, *Thorax*, 1946, **1**, 211).] *Donough O'Brien*

2789. **Collapse Therapy and the Bronchus**
L. E. HOUGHTON. *Tubercle* [*Tubercle*] **31**, 50–62, March, 1950. 23 figs., 19 refs.

Bronchial stenosis is an adverse mechanical factor in the evolution of tuberculous lesions from the primary complex to the advanced lesions of fibro-cavernous phthisis. An important aim in treatment is the re-establishment of free bronchial drainage. This may be achieved by bed rest, chemotherapy, antibiotics and/or collapse therapy. While taking advantage of the empirical effect of lung immobilization and relaxation, atelectasis must be avoided. Atelectasis as a complication of pneumothorax is a constant precursor of tuberculous empyema and is frequently associated with ultimate relapse. Adequate bed rest is an essential preliminary to pneumothorax in acute exudative lesions. Distension cavities are best closed by the reopening of partially stenosed bronchi. Collapse therapy is essentially a method of trial and error in this connexion and streptomycin may assist in securing an open bronchus. The irreversible procedure of thoracoplasty tends to re-establish bronchial drainage and cavities close more readily if this object is achieved. After the cavity has closed the drainage bronchi may become sealed off.—[Author's summary.]

2790. **Spontaneous Healing of Tuberculous Cavities: Mechanism and Frequency.** (La guarigione spontanea delle caverne tubercolari. Meccanismo e frequenza)
V. BARONI and L. VALLEGIANI. *Archivio "E. Maragliano" di Patologia e Clinica* [*Arch. "E. Maragliano" Pat. Clin.*] **4**, 985–1006, Sept.–Oct., 1949. 19 figs., bibliography.

The authors have investigated the incidence of spontaneous closure of tuberculous cavities in the lung in 790 male patients of an Italian sanatorium who were followed up in most cases for 10 to 12 months, but in some instances for several years. They were mostly awaiting thoracoplasty or had too extensive an infiltration for artificial pneumothorax treatment, and to this extent were selected. The cavities were of many different types and the general condition of the patients also varied considerably. In 39 cases the cavity seemed to close, as judged by clinical signs, sputum conversion (as determined by culture) and by the appearance of the standard chest *x*-ray film. But by taking tomographs with 1-cm. or even 0·5-cm. cuts residual cavities were found in all but 9 cases, so that true closure occurred in only about 1·1%. In 24 cases with "moderately old" cavities there was little alteration in size during the first 3 months or so of observation. During the next 3 or 4 months the cavity decreased to about one-third of its original size, after which there was little further reduction. In 5 cases the cavity seemed to disappear in a matter of weeks, but in only one of these was the disappearance confirmed by tomography. In the other 10 cases the course was variable. Cases of so-called "blocked cavities" were not included in the analysis.

[The proportion of closure found was probably affected by the selection of cases, but, as the authors point out, the possibility of spontaneous closure is only of interest in cases in which collapse measures are not possible.] *John Crofton*

2791. **On the Chemotherapy of Tuberculosis with Organic Arsenicals.** [In English]
N. HIRANO and M. MATSUI. *Kitasato Archives of Experimental Medicine* [*Kitasato Arch. exp. Med.*] **21**, 1–8, Nov., 1948. 2 refs.

2792. **The Present Status of the Chemotherapy of Tuberculosis with Conteben, a Substance of the Thiosemicarbazone Series**
A. MERTENS and R. BUNGE. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 20–38, Jan., 1950. Bibliography.

See also Sections Hygiene and Public Health, Abstract 2354; Radiology, Abstract 2491; Paediatrics, Abstract 2543.

MALARIA

2793. **The Response of the Cotton Rat to *Plasmodium berghei* (Vincke – Lips).** (Le comportement du cotton rat vis-à-vis du *Plasmodium berghei* (Vincke et Lips))
J. RHODHAIN. *Annales de la Société Belge de Médecine Tropicale* [*Ann. Soc. belge Méd. trop.*] **29**, 483–489, Dec. 31, 1949. 2 figs., 4 refs.

Although *Plasmodium berghei* develops in the cotton rat the infection is slight. Removal of the spleen either before infection or during the period of recovery from an acute attack produces an acute infection with death or a chronic infection of long duration. Chloroquine in a dose of 1·5 mg. per 10 g. of body weight cures the infection. *G. M. Findlay*

2794. **Proguanil-resistant Falciparum Malaria in Malaya**
J. F. B. EDESON and J. W. FIELD. *British Medical Journal* [*Brit. med. J.*] **1**, 147–151, Jan. 21, 1950. 9 figs., 18 refs.

In the early trials of proguanil ("paludrine") in 1946 it was found that *Plasmodium falciparum* was very sensitive to the drug, but it has since been shown that different strains of the parasite differ in proguanil-sensitivity and that considerable resistance may be developed in the course of treatment. Experimental trials of proguanil were begun at the Institute for Medical Research in Malaya early in 1947; naturally infected persons were admitted to the Tampin Malaria Branch of

the Institute and were given single doses of 100, 250, or 300 mg. of proguanil. If parasitaemia was still present 7 days later, or if therapeutic intervention before the seventh day was necessary, treatment was regarded as having failed; in 1947 there were no failures among 39 patients, in 1948 there were 4 failures among 61 patients, and in 1949 there were 17 failures among 72 patients. Detailed case-reports of 5 cases of failure are given.

So far as is yet known, resistance to proguanil seems to develop in the trophozoites and is transmissible through the gametocytes and sporozoites. In most of the resistant cases the patient came from a rubber estate where proguanil had been used for many months for mass suppression of malaria, and the authors suggest that this favoured the development of resistance. They think that it is important to use the drug for suppression in a more efficient and less haphazard manner than hitherto, and, where this cannot be ensured, that mepacrine or chloroquine should also be used, as these are not known to produce resistance in the malaria parasite.

J. F. Corson

2795. **The New Synthetic Antimalarial Drugs in Indo-China. Treatment and Prophylaxis of Malaria with "Nivaquine" (Chloroquine) and "Paludrine" (Proguanil).** (Les nouveaux antipaludiques de synthèse en Indochine: traitements curatif et préventif du paludisme par la nivaquine et la paludrine)

J. CANET. *Presse Médicale* [*Pr. méd.*] **57**, 1015–1017, Nov. 2, 1949. 38 refs.

"Paludrine" (proguanil) was first used in the treatment of malaria in Indo-China in 1947. "Nivaquine" (chloroquine, 7-chloro-4(α-methylbutylamino-δ-diethylamino) quinoline) and its closely related homologues, although first developed by the Germans in 1938 and in use in North Africa by 1941, first became available in Indo-China at the same time as proguanil, in 1947. The trials reported here were undertaken in a non-seasonal hyperendemic malarious region of North Cochin China whose population mainly consists of agricultural workers, the majority of whom have had malaria for a long time. [In France nivaquine is the name given to chloroquine.]

To compare the curative effect of the two drugs, two series of 140 cases of fresh infection with *Plasmodium falciparum* (85%) and *P. vivax* (15%) were treated, one with proguanil, the other with chloroquine, the daily dose of each drug being 0·30 g. The effect of the compounds was judged by the rapidity with which the temperature fell and the schizonts disappeared from the blood. Chloroquine was found to be more effective than proguanil. In malignant tertian fever, the fever disappeared on the 2nd day in some cases in both groups, but the proportion was much greater in that treated with chloroquine (61%) than with proguanil (36%). The schizonts usually disappeared on the 3rd or 4th day in 52% of those treated with chloroquine, compared with 40% treated with proguanil. On the evening of the 4th day blood smears were negative in 76% of the former group compared with 60% in the latter, and at the end of 5 days smears were positive in only 4% of the group receiving chloroquine compared with 10% of those receiving proguanil. In benign tertian malaria the fever usually disappeared on the 2nd or 3rd day in 75% of those treated with chloroquine compared with 35% treated with proguanil. At the end of the 3rd day 95% of the patients on chloroquine were afebrile compared with 70% on proguanil. This difference was maintained and by the end of the 4th day all the chloroquine-treated group were afebrile compared with 75% of the proguanil-treated. Chloroquine was thus found more effective than proguanil against *P. falciparum* and *P. vivax*, and, in 10 cases, against *P. malariae*. Both drugs were found to possess gametocyticidal effect, which was less marked against *P. falciparum* than against *P. vivax* and *P. malariae*. Both compounds were well tolerated in a daily dose of 0·30 g. for 5 or 6 days, and even in daily doses of 0·50 g. for 20 days or 1 g. for 5 days. This applied to children of 8 to 12 years as well as to adults. Side-reactions observed with proguanil (6 to 8%) were anorexia and slight nausea, and with chloroquine insomnia (5%). The optimum curative dose was 0·30 g. daily for 5 to 6 days for chloroquine or 6 to 7 days for proguanil. The smaller doses of proguanil advocated originally by British workers were found to be too low in a hyperendemic area.

Prophylactic trials were carried out on several thousand workmen and several hundred children. The dosage of each drug was 0·20 to 0·30 g. weekly, preceded in some cases by a preliminary curative course of 0·30 to 0·50 g. daily for 2 to 5 days. Chloroquine was found to be superior to proguanil, of which the weekly dose of 0·20 g. given on one or two occasions, as originally advocated, was found to be insufficient for hyperendemic areas. The most effective scheme of dosage with either drug was 0·30 g. for 3 to 5 days initially, followed by 0·30 g. twice weekly, then 0·30 g. once weekly. In more severe cases, 0·50 g. is given for 3 to 5 days followed by 0·50 g. twice weekly for 1 or 2 weeks, then a maintenance weekly dose of 0·30 g. when the acute symptoms of malaria had disappeared. It is suggested that association with gametocyticidal compounds like pamaquin may give even better results. Although in Indo-China chloroquine seems to be preferable to proguanil, its higher cost may restrict its use.

R. Wien

2796. **The Antimalarial Activity of 2, 4-Diamino-6, 7-Diphenyl Pterin; Its Potentiation by Sulfadiazine and Inhibition by Pteroylglutamic Acid**

J. GREENBERG. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **97**, 484–487, Dec., 1949. 9 refs.

The author tested six synthetic diaminopterins for antimalarial activity; he infected chicks intravenously with trophozoites of *Plasmodium gallinaceum* and gave the drugs by mouth, beginning a few hours before inoculation and continuing twice daily for 4 days. On the morning after the last dose the number of parasitized erythrocytes per 10,000 erythrocytes was counted; the smallest dose which reduced the mean parasitaemia by 75% was regarded as the minimum effective dose (MED). Only one of the compounds, 2 : 4-diamino-6 : 7-diphenyl-

pyrimido (4 : 5-d)pyrazine, numbered " DR 15791 ", showed antimalarial activity in tolerated doses; this was studied further. These diaminopterins had previously been reported to be antagonistic to pteroylglutamic acid (folic acid), so DR 15791 was given to chicks together with pteroylglutamic acid; 0·02 mg. of pteroylglutamic acid per g. twice daily diminished the antimalarial activity of DR 15791 given also in a dose of 0·02 mg. per g. twice daily, and 0·2 mg. per g. of pteroylglutamic acid had a rather greater inhibitory action, while 0·002 mg. per g. had no significant effect. The synthetic pterins had been shown by Daniels and Norris (*J. biol. Chem.*, 1947, **170**, 747) to increase the activity of sulphonamides against bacteria which synthesize their own glutamic acid; the author found that one-fourth of the MED of DR 15,791 with one-sixteenth of the MED of sulphadiazine showed antimalarial activity. Subeffective doses of sulphadiazine also activated maximum tolerated doses of two other diaminopterins.

DR 15791 was only about equal to quinine in action against *P. gallinaceum* and is therefore unlikely to be useful in human malaria; it behaves, however, very like chlorguanide (proguanil; " paludrine ") in relation to sulphadiazine and pteroylglutamic acid, and the author thinks that the two drugs have a similar mode of action, both being inactive *in vitro* but being changed in the body into similar active antimalarial substances.

J. F. Corson

2797. **Antimalarial Activity of Aureomycin Against *Plasmodium gallinaceum* in the Chick**

G. R. Coatney, J. Greenberg, W. C. Cooper, and H. L. Trembley. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 586–587, Dec., 1949. 3 refs.

The authors, working at the National Institutes of Health, Bethesda, Maryland, have studied the activity of aureomycin against *Plasmodium gallinaceum* in the chick. Birds were given doses of 18 to 150 mg. per kg. body weight by mouth twice a day for 4 days, beginning a few hours before inoculation with infected blood; on the following morning the parasitized erythrocytes were counted in blood smears. All the birds had developed the infection, but the number of infected erythrocytes per 1,000 was only from 4 to 80% of that found in control birds. The drug was judged to be about one-fourth as effective as quinine. Tests were also made against the exoerythrocytic forms of the parasite. A group of 30 chicks were inoculated intramuscularly with " one mosquito equivalent " of sporozoites; 20 were treated with aureomycin, 10 receiving doses of 75 mg. per kg. and 10 others 150 mg. per kg. twice a day for 4 days, the remaining 10 being controls. Another group of 45 chicks were inoculated with " 0·01 mosquito equivalent " of sporozoites, 15 being treated with 75 mg. per kg., 15 with 150 mg. per kg., and the other 15 being used as controls. In the first experiment 9 of the 10 controls died of an overwhelming exoerythrocytic infection; 7 of those receiving 75 mg. per kg. and 5 of those receiving 150 mg. per kg. became infected, but later than the controls, and only 5 of the treated birds died. In the second experiment all the 15 control chicks were infected and 11 died, while only 1 of the 30 treated birds died during the observation period of 35 days. In a test against the late exoerythrocytic forms 15 chicks were inoculated with " 0·01 mosquito equivalent " of sporozoites; 5 were given 100 mg. of aureomycin per kg. by mouth daily for 7 days, beginning when parasites first appeared in the blood (9 to 10 days after inoculation), and the other 10 birds were controls. An overwhelming exoerythrocytic infection killed 9 of the 10 controls and 1 of the 5 treated birds; the others, which were killed and examined after 31 days, showed no exoerythrocytic parasites.

These experiments showed that aureomycin can prevent death from exoerythrocytic infection with *P. gallinaceum* in the chick; the only other drugs known to do so are pamaquin, pentaquine, proguanil, and sulphadiazine. *J. F. Corson*

2798. **Aureomycin in Experimental Chesson Strain Vivax Malaria**

W. C. Cooper, G. R. Coatney, C. A. Imboden, and G. M. Jeffery. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **72**, 587–588, Dec., 1949. 2 refs.

Aureomycin was tried as a prophylactic against the Chesson strain of *Plasmodium vivax*. Two white male volunteers were infected by the bites of *Anopheles quadrimaculatus* and were given 1 g. of aureomycin every 3 hours for 7 days, beginning on the day of the mosquito bite. They developed malaria after 30 to 31 days, while 4 controls bitten by the same mosquitoes developed the disease 12 to 14 days, and 92 similarly infected controls in previous tests 10 to 16 days after being bitten. The delay is regarded as having been due to aureomycin.

The therapeutic action of aureomycin was tested in the above 4 controls, doses of 4 to 8 g. being given for 5 to 6 days; the parasitaemia increased and the fever continued until the fifth or sixth day, when there was a sudden great decrease in the number of parasites. Unfortunately, a course of quinine in daily doses of 2 g. for 7 days was started at the time of this decrease, but before it had been found by examination of the blood slides, so it is not known whether the blood would have become negative with aureomycin alone. The action of the drug on the erythrocytic forms, however, was far too slow for practical usefulness. Relapses occurred in all the 4 volunteers within 10 to 14 days after the end of quinine therapy, so aureomycin did not eradicate the tissue stage of this strain of *P. vivax*. *J. F. Corson*

2799. **An Epidemic of Malaria in the Kenya Highlands Transmitted by *Anopheles funestus***

R. B. Heisch and J. O. Harper. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **53**, 187–190, Sept., 1949. 4 refs.

2800. **Malaria. With Special Reference to Certain Experimental, Clinical, and Chemotherapeutic Investigations. Part I. The Life Cycle. Part II. Chemotherapy**

N. H. Fairley. *British Medical Journal* [*Brit. med. J.*] **2**, 825–830 and 891–897, Oct. 15 and 22, 1949. Bibliography.

History of Medicine

2801. **The Role of Disease in the 70,000 Casualties in the American Revolutionary Army**
J. E. GIBSON. *Transactions of Studies of the College of Physicians of Philadelphia* [*Trans. Stud. Coll. Phys. Phila.*] **17**, 121–127, Dec., 1949.

The author of this paper assembles evidence to indicate the severity of the casualties from disease in the American Army during the War of Independence. During the seven years of war the average American soldier, often ill-shod and poorly clad, offered little resistance to the prevalent forms of infection. It is not fully realized by the historians who have described that struggle that contagious disease accounted for ten times more deaths than did the guns of the well-equipped English army. The two diseases most dreaded were typhus fever and smallpox, but dysentery also took a heavy toll. In September, 1776, nearly 50% of the Northern Army was reported unfit for duty on account of sickness. Hospital accommodation was insufficient, and many who entered hospital with slight disorders became infected and died. Inoculation for smallpox was of little avail; vaccination had not then been discovered.

The present author gives details of the various epidemics, and describes the excellent services rendered by Morgan, Shippen, and other medical officers at a time when the death rate among the medical officers was greater than that of officers in the fighting forces.

Douglas Guthrie

2802. **Medical Service with the Roman Legions**
J. ELLIOTT. *New Zealand Medical Journal* [*N.Z. med. J.*] **48**, 585–590, Dec., 1949.

2803. **Neuropathology. An Historical Sketch**
G. B. HASSIN. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 1–17, Jan., 1950. 42 refs.

2804. **"The Doctors' Mob" of 1788**
J. C. LADENHEIM. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **5**, 23–43, Winter, 1950. Bibliography.

2805. **David Davis and the History of Obstetric Forceps**
J. BARNES. *University College Hospital Magazine* [*Univ. Coll. Hosp. Mag., Lond.*] **34**, 179–185, Dec., 1949. 12 figs., 10 refs.

[This is the text of a most interesting Presidential Address to the Maternity and Child Welfare Group of University College Hospital, London, given on October 24, 1949.]

David Daniel Davis was born near Carmarthen in 1777, the eldest son of a farmer. After taking his medical degree at Glasgow University he practised as a general physician in Sheffield from 1803 until 1813. He then moved to London and specialized in the practice and teaching of midwifery. In 1824 he was appointed as the first Professor of Midwifery in the University of London (University College). This post he held until 1841, the year of his death. Although Davis is perhaps one of the less familiar figures in obstetric history, the mere fact that he supervised the birth of Queen Victoria entitles him to some consideration. The tragic death of Princess Charlotte in childbed in 1817 had brought midwifery into the limelight, and Davis did much to restore the confidence of the public in this important branch of medicine. In 1825 there was published his "Elements of Operative Midwifery" and, in 1836, his "Principles and Practice of Obstetric Medicine" in two well-illustrated volumes. Davis was the first to describe phlegmasia alba dolens as due to phlebitis, and to show that puerperal sepsis might lead to peritonitis. The present paper is concerned chiefly with his association with obstetric forceps, of which instrument Davis invented several patterns—forceps with blades of unequal length, with a sliding lock, and with the right blade jointed. He made it a rule to use forceps only when natural powers had failed and when forceps delivery seemed preferable to all other methods, provided always there was sufficient room in the pelvis to permit of a live birth. In his view, forceps were applicable for a head presentation only and never for a dead child.

As a background to the practice of Davis, the author traces the well-known history of obstetric forceps from the time of the Chamberlens in the sixteenth century, with whom it remained a family secret for many years, to the days of William Smellie and William Hunter, which brings the story almost to the time of Davis. Present opinion would appear to be in favour of natural childbirth, with a freer resort to Caesarean section, now so safe under modern conditions, and a more conservative attitude towards forceps. The paper is illustrated by twelve figures and by a full-page portrait of David Davis which now hangs in Sheffield Royal Infirmary.

Douglas Guthrie

2806. **Anson Jones: Doctor and Diplomat**
T. W. CLARKE. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **50**, 65–68, Jan. 1, 1950. 7 refs.

2807. **Ashburton Thompson and the Plague. A Great Epidemiologist and his Triumph over the Black Death**
H. SUTTON. *Journal of the Royal Sanitary Institute* [*J.R. sanit. Inst.*] **70**, 73–76, Jan., 1950.

2808. **Francis Clifton and William Black: Eighteenth Century Critical Historians of Medicine**
M. NEUBURGER. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **5**, 44–49, Winter, 1950.

SUBJECT INDEX TO VOLUME 7

JANUARY—JUNE, 1950

References are to page numbers. An asterisk denotes title and reference only

Abscess of sweat glands, radiotherapy, 29
—, pulmonary, micropulverized penicillin in, 389
Acceleration, positive, physiological effects, 345
Acetaldehydaemia after alcohol ingestion, 463
Acetaldehyde formation after "antabus" and alcohol ingestion, 353
— metabolism after "antabus" ingestion, 353
— and metabolism of ethyl alcohol, 583
21-Acetoxypregnenolone in rheumatoid arthritis, 649
Acetylcholine, action of, 13
— in nerve conduction, 12
—, trimethylammonium group in, specificity of, 124
Acetylsalicylic acid in rheumatism, 405
Achlorhydria in diabetes mellitus, 371
Achondroplasia, spinal cord lesions in, 203
Acid–base balance, renal regulation, 120
Acidosis, ammonium chloride, renal compensation in, 120
—, diabetic, electrolyte balance in, 613
—, —, hypopotassaemia developing during treatment, 53
—, —, potassium metabolism in, 373
—, —, recurrent, emotional factors in, 262
—, —, serum potassium in, 262
Acne rosacea, liver function in, 295
Acrocyanosis, 268
Acrokeratosis verruciforme, 512
Acromegaly, glucose tolerance, 74
—, radon in, 355
Acronecrosis due to fibrin and endothelial-cell thrombi, 374
ACTH, *see* Adrenocorticotrophin
Actinomyces bovis, sensitivity to antibiotics, 42
Addison, Thomas, pioneer of endocrinology, 336*
Addison's disease, citric acid content of blood in, 76
— —, compound E in, 135
— —, deoxycortone in, 119, 643
— —, diabetes mellitus and, 76
— —, pregnancy in, 183
Adenitis, tuberculous, streptomycin in, 430
Adenoma, bronchial, 282
—, chromophobe, myth of, 598
—, pituitary, irradiation of, 244
Adenomatosis, pulmonary, 68, 175
—, — or infectious, 280
—, —, pathology, 500
—, —, sputum examination in diagnosis, 500
Adrenal cortex and arterial hypertension, 270
— — hyperfunction, salt tolerance test in, 505
— — in acute porphyria, 50
— — — pathogenesis of arthritis, 523
— — — psychoses, 654
— —, renal sodium excretion and, 343
— — secretion, blood glucose level and, 8
Adrenal cortex steroids, convulsion therapy and, 536
— — tissue, non-encapsulated, in periadrenal fat, 37
— -pituitary function, rheumatic disease and, 518
Adrenaline, action in isolated perfused lungs of dog, 121
—, — on heart rate, blood flow, and blood pressure, 575
— antagonism with alkyl homologues of ethylamines, 12
—, histamine liberation from isolated lung by, 574
—, intravenous, in headache, 526
—, optical isomers, acute toxicity, 12
—, skin reactions to, 49
— tolerance test in liver cirrhosis, 69
Adrenals, *see* Suprarenals
Adrenergic agents in bronchospasm, 279
Adrenocorticotrophin activity, screening test of chemical compounds for, 505
—, clinical effects, 523
— in asthma, 614
— — children with functional hypoglycaemia, 290
— — chronic rheumatoid arthritis, 522
— — disseminated lupus erythematosus, 511
— — — sclerosis, 525
— — Loeffler's syndrome and tropical eosinophilia, 642
— — myasthenia gravis, 412
— — rheumatoid arthritis, 407
— — — and acute gout, 306
— — —, gout, psoriasis with arthritis, and allergic disorders, 642
— — —, haematological changes, 648
— treatment, effects of, 641
Aerobacter aerogenes urinary tract infection, aureomycin in, 647
Aerosols of aluminium and sodium chloride, silica dust deposition in lungs and, 341
—, lung volume in health and, 11
Aerosporin, *see* "Polymyxin B"
Agglutination, centrifugal, 364
Agranulocytosis, chronic, 277
—, cyclical, 170
—, —, splenectomy in, 273
—, "diatrin" treatment and, 582
— due to drugs, 40
—, thiosemicarbazone treatment of tuberculosis and, 436
—, toxic, benzene treatment causing, 24
"AH - 289", pharmacological studies, 368
Air, bacterial flora, in underground trains, 561
—, compressed, bone lesions due to working in, 6
— disinfection by triethylene glycol, 561
— pollution in towns, respiratory disease and, 562
Air-sickness, *see* Motion sickness
Albumin, hydrolysed human serum, nutritive value, 230
Alcohol content of blood, post-mortem, medico-legal importance, 26
Alcohol, effect on liver after infective hepatitis, 180
—, — — —, prevention by choline, 595
— ingestion, acetaldehydaemia and electrocardiographic changes after, 463
— injection of nasal mucosa in hay-fever, 49
— poisoning in infants and children, 258
Alcoholism, "antabus" treatment, 584, 655
—, chronic, "antabus" treatment, 23
—, —, genetic control, 152
—, conditioned-reflex treatment, 416
—, drugs for, 584
—, liver biopsy in, 638
"Aleudrine" in bronchospasm, 279
— in dyspnoea of coal-miners, 279
— inhalation, effect on mucous membranes, 259
— test in diagnosis of bronchial asthma, 50
Alimentary tract, congenital obstruction of, 607
Alkali intake, calcinosis after, 51
Alkyl mercury compounds, poisoning by, 134
— phosphates, action on nerve–muscle preparation and central nervous system of cat, 123
Allergic disorders, 151–2, 259–60, 368–70, 485–6, 614–15
— —, adrenocorticotrophin in, 642
— —, vegetable gums and, 259
— —, vitamin therapy, 151
Allergy, 49–50
—, emotional conflict and, 614, 615
—, gastro-intestinal, treatment by "thephorin", 368
Allyl-*iso*propyl-acetyl-carbamide, *see* "Sedormid"
Alopecia, pituitary implantation in, 291
Altitude, effect of rapid ascent on man, 569
—, experimental tuberculosis and, 34
Aluminium dust aerosols, effect on silica dust deposition in lungs, 341
— monostearate, penicillin procaine with, use in children, 127
Amanita phalloides poisoning, endocrine treatment of adrenal insufficiency during, 23
Amenorrhoea, pituitary implantation in, 291
Amentia, naevoid, *see* Sturge–Weber's disease
"Amidone", *see* "Physeptone"
Amidopyrine, intravenous, in chronic articular rheumatism, 648
Amines, aromatic, bladder lesions due to, 116
Amino-acid assimilation by bacteria, 41
Amino-aciduria in uranium poisoning, 133
p-Aminobenzoic acid, antithyroid activity, 640
— — in chronic joint disease, 87
— — — tuberculosis, 438
— — — typhus fever, 543
Aminophylline in bronchospasm, 279
Aminopterin, bone marrow changes after, 386
—, haematological changes due to, 169
— in acute leukaemia, 108, 169, 382, 624
— — experimental neoplasms, 248
— — monocytic leukaemia, 275
— — sarcoma, 577
p-Aminosalicylic acid excretion, caronamide and, 437
— — in pulmonary tuberculosis, 217, 218, 327, 667
— — — urinary tuberculosis, 328
— —, streptomycin resistance of *Myco. tuberculosis* prevented by, 103
Ammonium chloride acidosis, renal compensations in, 120
— ions, quaternary, in nerve physiology, 13
Amoebiasis, 106–7
—, acute, conessine in, 106, 107
—, aureomycin in, 220
—, hepatic, chloroquine in, 106
— in Africans, treatment, 106
— — infancy, 556
—, thioarsenites in, 440
Amphetamine, effect on "curling" oesophagus, 634
— sulphate, intravenous, in acute barbiturate poisoning, 581
Amputations in sixteenth and seventeenth centuries, 448*
—, interscapulo-thoracic, in 1808, Ralph Cuming and, 560*
Amyl nitrite, effect on "curling" oesophagus, 634
Amyloidosis, secondary, 196
—, vitamin A in origin and prophylaxis, 474
β-Amylose, iodinated, *see* "Tridine"
Amyotonia congenita, 206
Anaemia, 62–5, 165, 275–7, 383–4, 496–7, 625–6
—, acute haemolytic, due to naphthalene poisoning, 353
—, arterial orthostatic, 160
—, arthritis and, in Simmonds's disease, 643
—, blood zinc content, 63
—, cobalt in, 343, 625
—, Cooley's, in Australia, 624
—, familial hypochromic, splenectomy and, 276
—, haemolytic, 167–8, 627–8
—, —, acquired, erythrocyte antibody production and, 64, 628
—, —, —, haemolysis in, 276
—, —, —, survival of transfused erythrocytes, 64
—, —, —, thrombocytopenia and leucopenia in, 628
—, — macrocytic, incomplete antibodies causing, 628
—, —, with panmyelopathy, 627
—, hypochromic, intravenous iron therapy, 625
—, intravenous iron–sucrose therapy, 62
—, macrocytic, associated with intestinal stricture and anastomosis, 166
—, —, experimental production, 166

Anaemia, megaloblastic, in coeliac disease, folic acid therapy, 275
—, —, of infancy, vitamin B_{12} treatment, 626
—, nutritional macrocytic, production in swine, 383
—, — —, vitamin B_{12} in, 276
—, — megaloblastic, 626
—, orthostatic, deoxycortone acetate and sodium chloride in, 76
—, **pernicious,** 165–7, 626–7
—, —, achylia gastrica in, 627
—, —, Addisonian, glossitis in, vitamin B therapy, 276
—, —, animal protein factor concentrate in, 166
—, —, haematopoietic activity of parenteral beef muscle concentrate in, 496
—, —, liver extract and folic acid antagonists in, 275
—, —, neurological complications in, folic acid therapy, 383
—, —, — —, vitamin B_{12} in, 412
—, —, of pregnancy, 626
—, —, out-patient treatment, 275
—, —, resistant to vitamin B_{12}, 627
—, —, serum proteins of, electrophoretic analysis, 62
—, —, teropterin and diopterin in, 383
—, —, thymidine in, 165
—, —, urinary phenol fractions in, effect of vitamin B_{12} on, 626
—, —, — renninogen in, 275
—, —, vitamin B_{12} in, 276, 626
—, —, — — and extracts of duodenal mucosa in, 165
— of pregnancy, intravenous iron in, 63
—, relation between carbonic anhydrase activity and zinc content of erythrocytes in, 63
—, sickle-cell, 496
—, —, radiological findings, 625
"Anahist", *see* "Neohetramine"
Anaphylaxis, eosinophilic response to, 151
Anastomosis, arterio-venous, in pulmonary circulation, 281
Anatomy, 229, 342
—, bibliography of Basle works on, 1537–1900, 448*
—, first Russian textbook, 559*
—, **morbid,** 598–600
— teaching and resurrectionist activities in N. Scotland, 559
Aneurin, physical efficiency and, 7
— pyrophosphoric acid, *see* Cocarboxylase
Aneurysm, aortic, thoracic and abdominal, dicetyl phosphate in, 272
—, arterio-venous, angiography in, 31
—, —, of lung, 67
—, cardiac, murmurs of, 376
—, intracranial, 201
— — carotid arterial, 653
—, mediastinal, angiocardiography in, 357
Angina pectoris, 56, 619–20
— —, aspirin in, 620
— —, emotional excitement and, 491
— —, papaverine in, 267
— —, stellate-ganglion block in, 56
Angiocardiography in diagnosis of pulmonary arteriosclerosis, 472
— — — — mediastinal tumour and aneurysm, 357
— — — — syphilitic aortitis, 472
Angiography, cerebral, in arterio-venous aneurysm, 31
—, —, rapid serial, 469
Angiography, percutaneous carotid, 469
—, — cerebral, 138
Anoxaemia, pulmonary, 174
Anoxia, *see* Oxygen deficiency
"Antabus", acetaldehyde metabolism after, 353
—, alcoholism treated by, 23, 584, 655
—, death following ingestion of alcohol after, 655
—, diabetes and, 655
—, diabetogenic effect, 463
—, site of acetaldehyde formation after, 353
"Antabus"–alcohol vascular reactions, 463
Anthelmintic drugs, kinetics of penetration through cuticle of *Ascaris*, 220
"Anthisan" and "phenergan", comparison, 49
—, therapeutic action, 78
Anthrax, cutaneous, 296
Antibiotics, 18–20, 348–51, 578–80
Antibody production, sites of, 146
— response in diabetes, relation of blood sugar and hypoproteinaemia to, 153
Anticoagulants in disseminated sclerosis, 200
— — venous thrombosis, 61
—, bis-3 : 3'-(4-oxycoumarinyl)-ethyl acetate, 577
—, 4-hydroxycoumarin, prothrombin time and, 576
Antimony compounds in schistosomiasis in mice, comparison, 221
— in multiple myeloma, 385
— poisoning, BAL in, 464
— preparations in mycosis fungoides, 512
"Antistin", dermatitis following, 644
—, therapeutic action, 78
Anuria, acute, conservative treatment, 197
— after ischaemia of renal cortex, 84
—, intrarenal lesions and, 197
Anal canal, carcinoma, *x*-ray therapy, 30
Aorta, abdominal, radiography in diagnosis of gastric ulcer, 31
— anomaly, right retro-oesophageal arch, 58
—, coarctation, abnormal digits, ovarian insufficiency, and shortness of stature associated with, 184
—, —, Adams–Stokes syndrome, complete heart-block and bicuspid calcareous aortic valve associated with, 58
—, —, clinical study, 162
—, —, isthmic, with patent ductus arteriosus, 618
—, —, patent ductus arteriosus and intrapulmonary vessels in, 247
—, —, sounds and murmurs in, 162
—, peroesophageal puncture, 470
—, stenosis of, calcified, 55
—, transposition of, and laevoposition of pulmonary artery, 58
Aortitis, chronic, phonocardiography, 377
—, syphilitic, angiocardiography, 472
—, —, mercuric cyanide treatment, 401
—, tuberculous, haematogenous tuberculosis and, 426
Aphasia in left-handed subjects after brain injury, 91
Apoplexy, epidemic, and poliomyelitis, 658
Arachnodactyly, case reports, 148
Arachnoiditis in posterior fossa, 310
—, segmental, spinal injuries and, 203
Arc welding, radiodermatitis of lip due to, 117
Arneth count, environmental variations in, 62
Arrhythmia, 56–8
—, auricular fibrillation, in normal hearts, 265
—, — —, exercise and, 57
—, — —, thyrotoxic, 57
—, — flutter, myocardial infarction and, 57
—, — —, sympathetic stimulation and, 158
—, cyclopropane anaesthesia causing, prevention, 15
—, gallop rhythm, 377
—, — —, phonocardiography of, 265
—, systematic physical and psychiatric examination in, 533
—, triple rhythm, 378
—, ventricular defects, effect of anoxia on, 57
Arsenic encephalopathy, BAL treatment, 23
— poisoning, BAL in, 464
—, radioactive, haematopoietic system disease and, 385
Arsenoxide preparations, syphilis treated by, 514
Arsphenamine, damage to nervous system, 308
"Artane" in Parkinsonism, 414, 530
— and related compounds, 125
Arterenol, *see* Noradrenaline
Arteries, carotid, thrombosis, 652, 653
—, intracranial carotid, aneurysm, 653
—, pulmonary, perbronchial puncture for contrast-medium filling, 470
Arteriography, pathological changes in arteries due to organic iodized compounds used in, 355
— in Raynaud's disease, 61
Arteriosclerosis obliterans as cause of leg ulcers, 622
—, pulmonary, angiocardiography, 472
Arteriostenosis, pulse-wave recordings in diagnosis, 493
—, rice diet in, 494
Arteritis, temporal, case reports, 162
Artery, carotid, acute blocking, 310
—, —, ligation, David Fleming and, 336*
Arthritis, adrenal cortex in aetiology, 523
—, anaemia and, in Simmonds's disease, 643
—, gonococcal, treatment, 85, 194
—, physiotherapy and, 466
—, procaine, intravenous, in, 519
—, **rheumatoid,** 519–23
—, —, 21-acetoxypregnenolone in, 649
—, —, adrenocorticotrophin in, 306, 521, 522, 642, 648
—, —, aetiology, 406
—, —, amidopyrine in, 648
—, —, anterior pituitary extract in, 523
—, —, aureomycin in, 198
—, —, children affected by, 85
—, —, chronic, subcutaneous nodules of, 87
—, —, copper salts and gold salts in, 85
—, —, cortisone acetate in, 407
—, —, deoxycortone acetate and ascorbic acid in, 522
—, —, foci of infection in, 407
—, —, gold salts in, 407
Arthritis, rheumatoid, granuloma annulare compared with, 299
—, —, haemagglutination test for, 520
—, —, hormones in, 522
—, —, joint function and, 85
—, —, pituitary implantation in, 649
—, —, plasma viscosity in, 252
—, —, post-partum plasma administration in, 648
—, —, "pregnenolone" in, 519
—, —, progesterone in, 648
—, —, serum proteins in, 648
—, —, steroid compounds in, 520
—, —, suprarenal cortex, role in, 293
—, —, synovial fluid biopsy in, 649
—, —, — examination and biopsy in, 405
—, —, therapeutic criteria, 85
—, —, ventricular function and blood values in, 520
—, —, *x*-ray treatment, natural resistance to infection and, 587
—, vertebral, tomography of, 245
Arthrography, opaque, of knee-joint, 141
Ascaris cuticle, kinetics of penetration by antihelminthic drugs, 220
— *lumbricoides* larvae, immunity of mice infected with, 222
Ascites, mechanism of, 501
Aspirin in angina pectoris, 620
— — vascular diseases, 620
— poisoning, 352
Asthma, adrenocorticotrophin in, 614
—, bronchial, "aleudrine" test in, 50
—, —, antihistaminic drugs in, 369, 486
—, —, electrocardiography, 485
—, —, "orthoxine" in, 369, 485
—, —, —, vital capacity during, 260
—, —, spirographic study, 151
—, —, succinic acid in, 151, 369
—, disseminated focal necrosis with eosinophilia and arteritis in, 50
—, mediastinal displacement in, 614
—, natural history, 370
—, specific desensitization in, control examinations, 260
Astrocytoma, *x*-ray therapy after aspiration biopsy, 470
Ataxia, nutritional spinal, cerebellar aspect, 487
Atelectasis, 629
Atheroma, pathogenesis, 474
Atherosclerosis, cholesterol-induced, 163
—, choline in prevention of, 272
—, lipid metabolism disturbance, 619
—, thiouracil producing, 163
Atom bomb casualties, pathology, 468
Atomic energy tests, beta-ray burns of hands in, 242
Atropine, antidiuretic effect, 16
—, hunger bradycardia and, 377
— in study of influence of heart rate on heart output, 618
Aureomycin, clinical trials, 237, 238
—, effect on herpes simplex virus in chick embryos, 578
—, — — pleuropneumonia-like organisms associated with rheumatism, 405
—, — — *Treponema pallidum*, 303
— in acute bronchitis of infants, 483
— — *Aerobacter aerogenes* infection, 647

Aureomycin in amoebiasis, 220
— — bacteriaemia, staphylococcal penicillin-resistant, 132
— — brucella infection, 131, 323, 662
— — — — in chick embryo, 438
— — colitis, chronic non-specific ulcerative, 288
— — dermatitis herpetiformis, 189
— — exanthematous typhus, 320
— — experimenta lpolyarthritis, 198
— — fibrocystic disease of pancreas with pulmonary involvement, 631
— — gonococcal and non-specific urethritis, 402
— — gonorrhoea, 193, 646
— — granuloma inguinale, 191, 513
— — herpes simplex, 189
— — — zoster, 537
— — influenza, 632
— — Kaposi's varicelliform eruption, 189
— — lymphocytic choriomeningitis, 419
— — lymphogranuloma venereum, bubonic form, 191
— — pertussis, 19
— — *Plasmodium gallinaceum* infection of chick, 671
— — pneumonia in infants and children, 237
— — —, primary atypical, 174, 237, 238, 631
— — —, — —, action on virus of, 657
— — psittacosis infection of chick embryo, 461
— — Q fever, 542
— — rheumatoid arthritis, 198
— — rickettsial diseases, 542
— — Rocky Mountain spotted fever, 97
— — septicaemia due to *Bacteroides funduliformis*, 324
— — staphylococcal infections, 238
— — syphilis, 303, 400, 401
— — —, late cutaneous, 19
— — tick-bite fever, 132
— — tularaemia, 324, 546
— — typhoid fever, 131
— — undulant fever, 439
— intravenous, 239
—, local, in painful mouth ulcerations, 390
Autism, early infantile, nosology and psychodynamics of, 207
Ayfivin, biological observations, 461

Bacilli, Gram-negative streptomycin-resistant, 145
Bacillus lactis aerogenes, see *Acrobacter aerogenes*
— *laterosporus*, antibiotics produced by, 18
Bacitracin aerosol, 350
—, evaluation and effects, 349
— in pyogenic infections, 188, 297
—, toxic effect on kidneys,, 349
Bacteria, 41–4, 144–5
—, amino-acid assimilation by, 41
—, penicillin, toxic effects of, 362
—, streptomycin sensitivity, 21
Bacteriaemia at onset of diphtheria, 211
—, penicillin-resistant staphylococcal, aureomycin treatment, 132
Bacterial infections, 99–101, 211–13, 321–5, 422–5, 543–7, 659–63
Bacterial infections, recurrent familial, eradication, 563
Bacteriophage types in penicillin-resistant staphylococcal infection, 253
Bacterium coli, streptomycin-resistant and -dependent strains, metabolic properties, 604
— *tularense*, effect of streptomycin and streptothricin on, 424
Bacteroides, clinical significance, 425
BAL in arsenical encephalopathy, 23
— in metal poisoning, 240, 464
" Banocide ", *see* " Hetrazan "
Banti's disease and related syndrome, 495
— —, differential diagnosis and treatment, 633
— —, Rh factor and, 289
Barbiturate narcosis in latent epilepsy, 313
— poisoning, amphetamine sulphate in, 581
— —, sodium succinate in, 581
Basle pamphlet on Theophrast von Hohenheim and on Paracelsian cosmology, 336*
" Bathers' itch ", schistosomal, 445
Bazin's disease, calciferol in, 582
B.C.G. diagnostic test, 325
— tuberculin, sensitivity tests of, 101
— —, B.C.G. - vaccinated subjects and, 225
— vaccination, after-effects in infants, 337
— —, efficacy, 114
— — in adolescents, 3
— — — older children, 2
— —, negative phase following, 113
— —, oral, results on 348 families, 548
— —, results of, 326
—, re-vaccination of school children, 2
Beef-muscle concentrate in pernicious anaemia, 496
Bejel, syphilis and, 301
" Benadryl ", serum - induced myocarditis and, 122
—, sulphamezathine and, in infantile gastro-enteritis, 149
Benzaldehyde thiosemicarbazone, *see* " TB I/698 "
Benzedrine, *see* Amphetamine
Benzene, toxic agranulocytosis due to, 24
Benzoic acid as thyroxine antagonist, 75
— —, effect on blood penicillin levels, and on renal function, 129
2-Benzyl - 4,5 - imidazoline, *see* " Priscol "
Beriberi, endemic, enriched rice in control of, 260
—, hydropic and cardiovascular, 153
Berylliosis, non-occupational, 452
Beryllium, cutaneous granuloma after contamination with, 116
— poisoning, experimental, 464
— worker, acute pneumonitis in, 6
Betatron, application in treatment, 138
Betz, Vladimir Alekseevich, 224*
Bile constituents, concentration in gall-bladder, 454
— flow in primary hepatitis, and in differential diagnosis of jaundice, 180
— pigments, elimination after transfusion of conserved blood and plasma, 24
Bilharziasis, *see* Schistosomiasis
Bilirubin blood level, sodium nicotinate and, 504
Biochemistry, 7–9, 119–20, 230–1, 343–5, 454–7, 567–9
Biography, medical, 112, 224, 336, 448, 560
Biopsy in tumour diagnosis, 38
Birth injury, *état marbré* of thalamus following, 203
— weight, physical development of children and, 365
Bismuth, gastroduodenal ulcer and, 503
—, oral, in dermatology, 295
— poisoning, BAL in, 464
— salicylate and penicillin in experimental syphilis, 645
— salts, sporadic goitres treated by, 75
—, syphilis treated with, 514
" Bistrimate " in dermatology, 295
Black, William, eighteenth-century medical historian, 672*
Blackwater fever, epidemiology in W. Africa (1941–5), 557
Bladder carcinoma, radiocobalt treatment, 138
— —, radium therapy, new technique, 244
— examination, tomography in, 592
— function disturbances and emotional stress, 654
—, irradiation injuries, late reactions, 470
— lesions due to aromatic amines, 116
— tumours in workers in chemical industry, 6
— —, malignancy, urographic assessment, 358
Bloating, non-gaseous abdominal, hysterical type of, 316
Blood, 250–2
—, adrenocorticotrophic activity, 294
—, alcohol content, post-mortem, medico-legal importance, 26
—, arterial, precooling, effect on acute cooling of hands and feet, 455
—, carbonic anhydrase activity in anaemia, 63
—, — — —, relation to zinc content of erythrocytes, 63
— cells, phase-contrast microscopy, 164
— —, *see also* Erythrocytes, etc.
— changes in liver cirrhosis, 164
— circulation, *see* Circulation
— clot, formation from purified bovine fibrinogen and thrombin, 568
— — retraction after " sedormid " purpura, 497
— — — in menstruation, 7
— coagulation, co - thromboplastin assay, 250
— —, effect of penicillin on, 130
— —, — — protamine on, 459
— — in hyperglobulinaemia, 624
— — — leukaemia and polycythaemia, 360
— — — thrombocytopenic purpura, 168
— —, post-operative, in congestive heart failure and thrombophlebitis, 251
— — time, effect of streptomycin on, 22
—, diphtheria toxin content, in late diphtheria paralysis, 211
— **disorders,** 62–6, 164–71, 273–8, 382–7, 495–8, 624–8
—, erythrocyte count, high-altitude flying and, 569
— flow, adrenaline and its derivatives and, 575
— —, arrest in arm, sensation disturbances in hand after, 569
— —, cerebral, dihydroergocornine and, 574
Blood flow, coronary, in simulated emotional excitement, 491
— —, —, measurement in man, 157
— —, —, reduction in, electrocardiographic changes, 154
— — to fingers, variations in health and disease, 379
— —, peripheral, in chronic lupus erythematosus, 511
— —, —, tetraethylammoni u m chloride and, 268
— —, renal, and glomerular filtration rate in congestive heart failure, 375
— —, —, response to graded partial obstruction of renal vein, 36
— gas analysis, cardiac and arterial, in cardiac disease, 376
— glucose level, adrenal cortex secretion and, 8
— group A, relation to Rh immunization and haemolytic disease of newborn, 384
— —, antibody anti-S, haemolytic transfusion reaction due to, 135
— —, B factor, brain damage in child after maternal isoimmunization, 484*
— —, immunochemical studies, 567
— —, Rh agglutinins, anamnestic reaction with, 241
— —, — antibodies, clinical significance, 25
— —, — — anti-C^{w}, production by immunization, 64
— —, — factor, Banti's disease and, 289
— —, — —, iso -immunization against, 241
— —, Rh-negative woman already sensitized, intensive immunization of, 167
— — substances A and B, preparation from human saliva and horse stomach, 567
— in faeces, occult, tests for, 602
— iodine, micro-determination, 567
— penicillin concentration in syphilis, 516
— — level, benzoic acid and caronamide and, 129
— plasma, electrophoretic, nitrogen, and lipid analyses, 361*
— —, post-partum, albumin and globulin content and use in rheumatoid arthritis, 648
— —, stored, stability of prothrombin and Ac-globulin, 456
— — viscosity in pulmonary tuberculosis and rheumatic diseases, 252
— — — — rheumatic diseases, 405
— platelet adhesiveness in thrombo - embolism and haemorrhagic disease, 272
— — changes in thrombo-embolism, 490
— — count in wide-field *x*-ray therapy, 589
— — thrombosis, generalized, 274
—, preserved, malarial parasites in, 25
— pressure, arterial, actions of adrenaline and derivatives on, 575
— —, deoxycortone acetate and, 83
— —, diastolic, transient disturbance in upper limbs, 55
— — in essential hypertension, protein deficiency and, 622
— — — menopause, 270
— —, physical fitness and, 567
— —, portal venous, indirect estimation, 501

Blood pressure pulmonary capillary venous pulse, 230
— — regulation, dimethyl-tubocurarine and, 15
— —, renal venous, increased, 36
— —, venous and right auricular, posture in determining, 343
— serum albumin, crystalline bovine, effect of lithium periodate on, 41
— —, esterified fatty acid levels of, 230*
— —, iron level of, effect of iron therapy on, 496
— — of horse, massive injections in rabbits, 33
— — proteins in blood dyscrasias, electrophoretic analysis, 62
— — — structure and liver function in gout, 52
— —, thermolabile component, combination with viruses, 477
—, "sludged", in allergy, 486
— stains in pregnancy, Galli Mainini reaction, 467
— sugar level, pituitary growth hormone and, 119
— —, post-mortem, 26
— —, relation to antibody response in diabetes, 153
— temperature, arterial, in resting forearm, 456
—, thiouracil and thiourea effect, 273
— transfusion, elimination of biliary pigments after transfusion of conserved blood and plasma, 24
— —, exchange, after incompatible blood administration, 585
— —, —, in acute catatonia, 94
— —, —, — — leukaemia, 624
— —, —, — diseases other than haemolytic disease of newborn, 466
— —, —, — erythroblastosis foetalis, 47
— —, —, — haemolytic disease of newborn, 64
— —, group O, use of group-specific substances in, 135
— —, haemolytic reaction due to antibody anti-S in, 135
— —, haemosiderosis aggravated by, 25
— — in nephrogenic hypoproteinaemia, 84
— — — prolonged insulin coma, 489
— — — shock due to myocardial infarction, 619
— —, James Blundell and, 560*
— —, myocardial infarction and, 158
— —, placental, 24
— —, shock prevention by procaine, 241
— —, water exchange after, 466
— **vessels,** 61, 162–3, 271–2, 622–3
— — reactions in fingers to local cooling, 568
— —, upper limb, after sympathectomy, 163
— volume increase in physical training, 455
— —, pulse rate and cardiac volume during rest and, 455
Blundell, James, and blood transfusion in man, 560*
Boeck's sarcoid, *see* Sarcoidosis
Bologna Medical School, historical and biographical notes, 224*
Bone changes in erythroblastosis foetalis, 140
—, cryptococcosis involving, 656
— growth after encephalitis lethargica, 202
— —, diathermy and, 241
Bone lesions in congenital syphilis, 82
— — — sarcoidosis, 246
— — — workers in compressed air, 6
— marrow blood, sternal, in polycythaemia vera, oxygen saturation, 277
— — changes after aminopterin, amethopterin, and aminoanfol, 386
— — — in liver cirrhosis, 164
— — in renal disease, 624
— —, sternal, biopsy in malignant lymphoma, 66
— —, —, in periarteritis nodosa, 61
— —, —, tissue mast cells in, 495
— —, thiouracil and thiourea and, 273
— metastasis in malignant melanoma, 358
—, radium deposits in, 137
— tumours of cranial vault, radiological diagnosis, 590
Borrelidin, enhancement of penicillin activity by, 18
—, experimental trials, 18
Bradycardia due to starvation, effect of atropine on, 377
Brain, 91–3, 200–3, 309–12, 526–8
—, cavum septi pellucidum, clinical picture in dilatation of, 527
— circulation, *see* Circulation,
—, cisternal puncture, mishaps due to, 526
— cortex in central nervous regulation of cardiovascular function, 9
— damage after pertussis vaccine prophylaxis, 527
— disease, organic, psychological problems of children with, 207
— —, pneumotherapy in, 535
—, dura mater, nerves of, role in headache, 200
— glioma, radiotherapy, 588
— —, — at operation for, 471
— haemorrhage, thrombosis, and embolism, factors affecting prognoses, 527
— injuries after spontaneous delivery at full term, 257
— —, aphasia in left-handed subjects after, 91
— —, growth and sexual development and, 526
— — in ancient Egypt, 111
— —, test performance in, 532
— lesion, acute necrotizing haemorrhagic, 92
— — due to intracranial aneurysms, 201
— —, electroencephalographic wave patterns and, 409
— — produced by deoxycortone acetate, age factor in, 294
—, neostriatum, palaeostriatum, and neighbouring structures, electrical activity in Parkinsonism and hemiballismus, 199
—, olivo-ponto-cerebellar atrophy, 310
—, posterior fossa, meningioma of, 528
—, senile, acid phosphatase in, 309
— thrombosis and embolism, stellate ganglion block in, 652
— tuberculoma, tuberculous meningitis and, 329
— tumours, electroencephalogram in, 199
—, vascular occlusion in, nature of infarcts following, 33
— weight and changes in schizophrenia, 534
Breast, *see also* Mammary
Breast carcinoma, operation after-effects, radiotherapy in, 589
— feeding, post-war incidence, 479
Brödel's ulnar palsy, historical notes, 560*
Bromide intoxication, 583
— —, nicotinamide treatment, 583
Bronchiectasis in childhood, 367
—, segmental distribution of lesions in, 388
Bronchiolitis, acute, in infants, aureomycin in, 483
Bronchography with "ioduron B", 590
Bronchopneumonia, epidemic, in man and animals, 542
—, tuberculous, in childhood, streptomycin in, 104
Bronchopulmonary lithiasis, active, 172
Bronchoscopy in tuberculous children, 150
Bronchospasm, adrenergic agents in, 279
—, aminophylline in, 279
Bronchus, adenomata of, 282
—, carcinoma, co-existence with active pulmonary tuberculosis, 175
—, —, cytological diagnosis, 282, 600, 632
—, —, nitrogen mustard treatment, cytological changes after, 38
—, —, oil particles in lung and development of, 632
—, —, tomographical diagnosis, 139
—, congenital obstruction, 255
— function, dynamics of, 172
—, indices of elasticity and pulmonary ventilation during attack of bronchial asthma, 151
— infections, segmental, 389
—, intramural nervous system, changes in pulmonary tuberculosis, 474
— lavage in pulmonary tuberculosis, 554
—, main, tuberculosis of, 547, 555
—, pneumothorax and, 669
— secretions, cytohistological study, 68
— —, tumour cells in, 68
Brucella, effect of aureomycin and streptomycin on, 131
—, — — —, —, and chloramphenicol on, 323
—, killed, effect of ingestion on formation of antibodies, 663
Brucellosis, 438–9
—, aureomycin in, 323, 439
—, chloramphenicol in, 323
—, chronic, aureomycin in, 662
—, —, chloramphenicol in, 662
—, experimental, appearances in eye, 475
—, —, polymyxin treatment, 552
—, gold therapy, 439
—, haemorrhagic forms, 438
— in chick embryo, aureomycin treatment, 438
Burned buildings, medico-legal examination of bodies recovered from, 27
Burns, beta-ray, of hands during atomic energy tests, 242
—, cutaneous, due to fluorescent light, 227
Butterfly wing extract, antibiotic for malaria, 219
Bynoe, Benjamin, surgeon of H.M.S. *Beagle*, 448

Calciferol, danger in infants of large doses, 479
— in erythema induratum, 582
Calciferol in lupus vulgaris, 188, 511
— — psoriasis, 79, 81
— — sarcoidosis, 625
— — tuberculous conditions of skin, sarcoidosis, granuloma annulare, psoriasis, and lichen planus, 79
— -treated lupus vulgaris, histological changes and non-irradiated ergosterol in, 511
— treatment, polyneuritis as complication of, 644
Calcification of aortic valve, clinical and radiological features, 55
—, "egg-shell", in silicosis, 172
— in bronchi and lungs, 172
— — intraspinal meningiomata, 245
—, premature, of ribs, 306
Calcinosis after prolonged intake of milk and alkali, 51
Calcium ascorbate, effect on vascular permeability and vitamin-C metabolism, 232
— phosphate, adsorbent complex in peptic ulcer therapy, 176
— succinate in rheumatism, 405
Calculus formation in lung, 67
"Camoquin hydrochloride", antimalarial action, 109
Cancer specialist of 100 years ago, odyssey of an American, 224*
Candida in sputum from pulmonary tuberculosis, 363
Canicola fever, differential diagnosis, 417
— —, fatal case, 209
— — in Germany, 209
Capillary fragility during dicoumarol therapy, 16
— —, effect of epicatechin and ascorbic acid on, 497
— permeability in allergy, dermofluorometer in study of, 49
"Carbitol solvent" and "carbitol", effect on human skin, 186
Carbohydrate metabolism and gastric secretory activity, 502
— — in relatives of diabetics, 261
— — — Wilson's disease, 203
— —, physiology and pathology, 359
— —, thiopentone anaesthesia and, 121
— —, venous catheter technique in study of liver in, 372
Carbon dioxide snow, contact dermatitis treated by, 78
— monoxide, endogenous formation in man, 457
Carbonic anhydrase activity of blood in anaemia, 63
— — — — —, relation to zinc content of erythrocytes in normal, anaemic, and other pathological conditions, 63
Carcinoma, choline therapy, 460
—, cutaneous, of face, history, 224*
—, gonadotrophin excretion in diagnosis, 249
— growth, aminopterin and, 248
—, malignancy at different ages, 3
—, mammary, in mouse, isolation of virus, 596
— metastases, anatomical distribution in rabbit, 597
—, nitrogen mustard analogues in treatment, 577
—, osmotic resistance of erythrocytes from patients with, 249
—, serum polysaccharide level in, 249
— tissue sensitivity, irradiation-induced mitotic changes and, 28
— treatment, results of, 564

Cardiospasm, 284
—, effects of drugs on clinical and radiological picture, 178
Cardiovascular disorders, 54–61, 154–63, 263–72, 374–81, 490–4, 616–23
— — due to pulmonary embolism, 374
— function, central nervous regulation, role of cerebral cortex in, 9
— — and work performance, effect of rest in bed, 611
— system in toxaemias of pregnancy, 616
Caries, dental, dietary control, 149
Caronamide, effect on *p*-aminosalicylic acid excretion, 437
—, — — blood penicillin levels and renal function, 129
—, plasma penicillin concentration, 20
Carotid sinus pressor response in hypertension due to compression of renal arteries, 59
— — syndrome, ocular symptoms in, 380
— — —, physiological basis of consciousness and, 527
Casualties due to disease in American Army during War of Independence, 672
Catatonia, acute, exchange transfusion in, 94
—, — fatal, 535
Catheterization of coronary sinus in man, 54
Cell nucleus structure in prolonged protein insufficiency, 476
"Cellothyl" *see* Methylcellulose
Centaur, Chiron the, 335
Cerebrospinal fluid, antibacterial action of streptomycin inhibited by, 21
— —, antibiotics in, 21
— —, diphtheria toxin content in late diphtheria paralysis, 211
— — during streptomycin treatment of tuberculous meningitis, 432
— — in herpes zoster, electron microscopic study, 318
— — — syphilis, 303
— —, penicillin levels in, 129, 351
Cervix uteri, *see* Uterus, cervix
Cesalpino's role in history of medicine, 224*
Cestodes, chloroquine treatment, comparison with other vermifuges, 537*
"Chancre", evolution of term and relation to history of syphilis, 447
Cheilitis, chronic, 190
Chemical industry, bladder tumours in workers in, 6
Chemotherapy, 16–17 126–7, 234–5, 460–2, 577–8
Chest tumours, solitary, differential diagnosis, 139
Cheyne, George, 1673–1743, 560*
Chickenpox and herpes zoster, co-existence of, 209
Chiron the centaur, 335
Chloramphenicol, action on *Brucella*, 323
—, — — virus of primary atypical pneumonia, 657
—, clinical trials, 237
— in acute gonorrhoeal urethritis, 402
— — atypical pneumonia, 282
— — brucellosis, 323
— — chronic brucellosis, 662
— — early syphilis, 514, 646
— — encephalitic typhoid, 349
— — enteric fever, 321
— — experimental rickettsial infection, 420
— — *fièvre boutonneuse*, 543
Chloramphenicol in gonorrhoea, 513, 514
— — infantile gastro-enteritis, 481
— — paratyphoid B fever, 661
— — — in infants and young children, 544
— — pertussis, 661
— — psittacosis infection of chick embryo, 461
— — salmonella enteritis, 662
— — salmonellosis, 131
— — scrub typhus, 421
— — tsutsugamushi disease, 320
— — typhoid fever, 131, 237, 321, 322, 422
— — — and paratyphoid B, 660, 661
— — — carriers, 543, 544, 661
—, sulphadiazine and, in experimental typhoid, 349
Chloroquine diphosphate in malarial splenomegaly, 331
— in clonorchiasis, 444
— — falciparum malaria, 444
— — giardiasis, 441
— — hepatic amoebiasis, 106
— — malaria, 219, 670
Chlorvinyl plastics, hygiene of production of, 453
Cholecystography, electrocardiography of patients given "pitressin" for, 158
Cholera, "thalamyd" in, 213
Cholesterol content of coronary artery and blood in acute coronary artery thrombosis, 619
— feeding, atherosclerosis produced by, 163
Choline deficiency, renal lesions due to, 596
—, effect on changes in liver and body fluids during protein depletion, 289
—, prevention of experimental atherosclerosis and, 272
— — of liver damage due to alcohol or sugar, 595
— therapy of carcinoma, 460
— — of fatty infiltration of liver, 394
— — — ichthyosis, 644
Cholinergic compounds, interrelationship of, 460
Cholinesterase inhibition and plasma neostigmine levels in dogs and myasthenic patients, 11
Choriomeningitis, acute lymphocytic, 651
—, lymphocytic, aureomycin in, 419
Circulation, cerebral, bilateral stellate ganglion block and, 160
—, —, effect of posture on, 653
— **disorders,** 59–61, 160–1, 267–9, 379–80, 493–4, 620–2
—, dihydroergocornine and, 268
—, noradrenaline and, 460
— in pulmonary anoxaemia, 174
— — — tuberculosis, 555
—, peripheral, in convulsion therapy, 317
—, —, local short-wave diathermy and, 354
—, —, pentamethonium iodide and, 272
—, —, "priscol" and, 13
—, pulmonary capillary venous pulse pressure, 230
—, —, in health and left ventricular failure, 263
—, regional, radioactive sodium in measurement of, 267
—, renal, 517
—, —, neurovascular control of, 517
— times in congenital heart disease, 59
— —, lobelline determination, 616
—, *x* rays and, 468
Circulatory system, 455–6
Circumcision and venereal disease, 300
Citric acid content of blood in Addison's disease, 76
Clifton, Francis, eighteenth-century medical historian, 672*
"Ciradon", clinical trials and pharmacological properties, 571
Clonorchiasis, chloroquine in, 444
Clostridium welchii collagenase, effect of alkaline *p*H and heat on, 144
Coal-tar foodstuff dyes, carcinogenic effects, 449
Cobalt, anti-anaemic action, 625
—, erythropoietic effect in health and anaemia, 348
—, radioactive, in malignant visceral tumour, 138
Cocaine, anoxic vasoconstriction and, 574
Cocarboxylase in diabetic coma, 371
Coccidioidomycosis, disseminated, and lymphohaematogenous tuberculosis, 109
—, —, coexistence with tuberculosis, 417
—, persistence of residual pulmonary lesions of, 172
Codeine poisoning, facial oedema in, 134
Coeliac disease, 610
— —, fat absorption in, 610
— —, megaloblastic anaemia in, treatment, 275
— —, principal features, 502
— syndrome, development of, 47
— —, dietary starch and fat absorption in, 47
— —, hypothyroidism in development, 47
Coke fires, pneumoconiosis from dust of, 566
Colchicine, effect on *Plasmodium vivax*, 443
— treatment of progressive muscular atrophy, 412
Cold, common, *see* Common cold
Colitis, segmental, rheumatic fever and, 334
—, ulcerative, chronic, aureomycin in, 288
—, —, —, carcinoma and, 393
—, —, — idiopathic, hyperalimentation in, 288
—, —, —, nitrogen metabolism in, 288
—, —, idiopathic, early radiological changes, 140
—, —, in children, 607
—, —, pathogenesis, 474
Collagenase of *Cl. welchii*, effect of alkaline *p*H and heat on, 144
Collins, *Sir* William, surgeon and statesman, 560*
Colloidal red test as index of liver function, 39
Colon, diverticulitis of, 30
— function, methylcellulose and, 393
Colostrum, immunology of, 44
Coma, diabetic, cocarboxylase in, 371
Common cold, γ globulin in, 210
— —, histamine antagonists in, 539
— —, "neohetramine" in, 658
— —, phenindamine in, 539
"Compound E", *see* Cortisone acetate
Conessine in acute amoebiasis, 106, 107
Congenital anomalies, recurrence in siblings, 118
Conglutination phenomenon, choice of complement for, 478
Consciousness, carotid sinus syndrome and physiological basis of, 527
Consciousness, electric convulsion therapy and, 536
Constipation, sodium carboxymethylcellulose in, 394
Contagious diseases, specific therapy and, 338
"Conteben", *see* TB I/698
Contrast media, hyaluronidase to accelerate spread and absorption, 29
Convulsions, drugs for, 10
—, electrically induced, electroencephalogram in, 525
—, induced, decamethonium iodide and, 11
— in infancy, 256
Copper and copper–arsenic poisoning, BAL treatment, 240
— salts in disseminated sclerosis, 90
— — — rheumatoid arthritis, 85
Coproporphyrin in infective hepatitis, infectious mononucleosis, and mechanical jaundice, 39
— in normal urine, 152
—, urinary, relation of haemoglobin and of bacterial metabolism in intestinal tract to, 152
Coproporphyrinuria, idiopathic, 152
Cor pulmonale, chronic, neurological effects of oxygen in, 491
— — in silicosis, 264
— —, subacute, pathology in diffuse carcinomatosis of lungs, 142
Coramine, *see* Nikethamide
Coronary artery occlusion, loss of myocardial contractility after, 378
— **disease,** 378–9
— —, clinical and epidemiological study, 450
— —, exercise test in diagnosis, 56
— **occlusion,** 56, 619–20
— —, chronic rheumatic heart disease and, 619
— sinus catheterization in man, 54
— thrombosis, heparin in Pitkin menstruum in, 56
— —, infarction of interventricular septum and right ventricle, electrocardiographic and pathological findings, 56
Corticoids, salt-active, in pathogenesis of hypertension, 60
Cortisone acetate in hypertension, Addison's disease, and diabetes mellitus, 135
— — — rheumatic fever, acute phase of, 110
— — — rheumatoid arthritis, 407
— and production of granulation tissue in rabbits, 643
—, review of clinical effects, 523
— in rheumatoid arthritis, 523
Corynebacterium diphtheriae, cultural toxicity and virulence, 212
— — growth, pancreatic extract stimulating, 254
— *endocarditis* isolated from "abacterial" endocarditis, 144
Cosmic radiation, influence on experimental tuberculosis, 34
Co-thromboplastin assay in study of blood coagulation abnormalities, 240
Cotton fibres, pulmonary artery reactions to emboli of, 476
Coxsackie viruses, differentiation of strains, 658
Cramp due to heat, 485
— — — prolapsed intervertebral disk, 409
Cretinism, electrocardiogram in, 264

Crohn's disease, streptomycin in, 393
Cross-infection, incidence in children's wards, 365
" Cryogenine ", antipyretic action, 570
Cryotherapy in contact dermatitis, 78
Cryptococcosis, bone involvement in, 656
—, cutaneous, 296
" Crysticillin ", aqueous injection, 351
Cuming, Ralph, and interscapulothoracic amputation, 560*
" Cupralene " in rheumatoid arthritis, 85
Curare, action on central nervous system, 458
— and exercise in anterior poliomyelitis, 210
—, effect on electroencephalogram of rabbit, 570
— treatment of muscle spasm in rheumatic disorders, 405
— — — phlebitis, 490
Cushing's disease, *see* Pituitary basophilism
Cyanosis, chronic, in atrial septal defect, 492
Cyclopropane anaesthesia, arrhythmia during, 15
Cytology, 342

" Dacorene ", cardiotoxic properties of " 2489 F " inhibited by, 352
Darier's disease, liver function in, 80
" Darvisul ", *see* Phenosulfazole
Daviel on the *noli-me-tangere*, 224*
Davis, David, and history of obstetric forceps, 672
Daylight, experimental tuberculosis and, 34
DDT dusting, domestic rats and, 29
—, residual insecticide against *Anopheles gambiae*, 586
— spray in controlling filariasis, 135, 136
— — — — flies, 115
— — in sandfly eradication, 337
Deaf-mutism, genetic investigation, 118
Deafness in children, heredity and rubella in, 255
Death, ether sign of, 27
— in infancy, unexpected, 46
Decamethonium iodide, effect on respiration and induced convulsions, 11
Decamethylene - 1 : 10 - bis - trimethylammonium bromide, curariform action, 458
Dehydration of infants, hyaluronidase with subcutaneous fluid infusion in, 366
11-Dehydro-17 - hydroxy - corticosterone acetate, *see* Compound E
Dehydroergotamine methanesulphonate for herpes zoster pain, 657
Delinquency, juvenile, intelligence and, 26
Dentists, allergic contact dermatitis in, 296
Deoxycortone acetate, articular lesions produced by, 293
— —, ascorbic acid and, in rheumatoid arthritis, 522
— —, brain lesions produced by, 294
— —, effect on blood pressure and nephrosclerosis, 83
— —, — — experimental hypertension, 620
— —, — — production of vascular lesions, 60
— —, — — sodium, potassium, and water excretion in dog, 290
Deoxycortone acetate in Addison's disease, 119, 643
— — — *Amanita phalloides* poisoning, 23
— — — infective hepatitis, 658
— —, pitressin and, antagonistic actions, 290
— —, sodium chloride effect on action of, 183
— —, — — and, in postural hypotension and orthostatic anaemia, 76
— —, vascular diseases due to, 359
Dermatitis, contact, cryotherapy, 78
—, —, liver function in, 295
—, —, procaine causing, 296
— herpetiformis, aureomycin in, 189
— —, chronic eczema as variant of, 398
—, " pyribenzamine " and " antistin " as causes of, 644
—, suboccipital, 398
Dermatology, 78–81, 186–90, 295–9, 398–9, 509–12, 644
Dermatomycosis, biochemical changes in sweat in, 79
—, ethyl mercury phosphate in, 78
Dermatomyositis, forms of, 186
Dermatosis in old age, 509
Dermis, fibrous changes in, in senile elastosis, 299
Dermofluorometer in study of capillary permeability in allergy, 49
Dermis, in senile elastosis, 299
Dermofluorometer in capillary permeability in allergy, 49
Desoxycorticosterone, *see* Deoxycortone acetate
Dextrose, *see* Glucose
Diabetes, 52–3, 261–2, 371–3, 612–14
—, acidosis and ketosis, electrolyte balance in, 613
—, —, serum potassium in, 262
—, " antabus " in, 463
—, — contraindicated in, 655
—, antibody response in, 153
— coma, cocarboxylase in, 371
— in children, 257, 610
—, glomerulosclerosis in, 613
— insipidus, pituitary implantation in, 291
— —, pituitrin and polyvinylpyrrolidone in, 185
—, latent, in relatives of diabetics, 261
— mellitus, achlorhydria in, 371
— — and Addison's disease, 76
— —, compound E in, 135
— —, external ocular muscular palsies in, 53
— —, glucose tolerance tests in, 74
— — in children, 489
— — — U.S. army, 1941–4, 489
— —, intercapillary glomerulosclerosis in, 153
— —, Kaposi's disease with, 644
— —, renal lesions in, 403
— —, " undulating ", 261
— —, —, vitamin E in, 489
—, staphylotoxin immunity in, effect of specific anatoxin on, 44
—, vitamin B in, 373
4,4'-Diaminodiphenyl sulphone in lepromatous leprosy, 659
Diaminopterin, synthetic, anti-malarial activity, 670
" Diaparene " in skin treatment in incontinence, 398
Diarrhoea, infantile, " formocibazol " in, 255
—, —, with vomiting, streptomycin in, 256
—, pathogenicity of organisms in, measurement of, 565
Diathermy, short-wave local, effect on peripheral circulation and tissue temperature, 354
—, — and micro-wave, bone growth in rat and, 241
" Diatrin " hydrochloride, clinical and toxicological studies, 369
— treatment, agranulocytosis during, 582
Diazomethane poisoning, 582
" Dibenamide ", sympatholytic effect, 268
" Dibenamine ", effects on mammalian heart, 572
— psychosis, 315
Dibromsalicil, bacteriostatic effect, 234
—, trial in animals, 127
—, wounds treated with, 234
" Dibutoline ", ganglionic blocking action, 12
Dicetyl phosphate in aneurysm of thoracic and abdominal aorta, 272
Dichloroxyquinaldine, topical, in dermatoses, 398
Dicoumarol in congestive heart failure, 347
— therapy, 584
— —, capillary fragility and, 16
— —, control of, 476
" Dicuprene " in rheumatoid arthritis, 85
Dienoestrol, clinical evaluation, 291
Diet in dental caries, 149
— — experimental uraemia, 195
Dietetics in sixteenth and seventeenth centuries, 559*
Diethylaminoethanol, haemodynamic properties, 125
Diethylaminoethyl-N-thiodiphenylamine hydrochloride, *see* " Diparcol "
Diethyl *p*-nitrophenylthiophosphate, *see* " Parathion "
Diethylstilboestrol in mumps orchitis, 318
Digestive disorders, 69–73, 176–81, 283–9, 390–5, 502–4, 633–9
Digitalis glucosides, vagus effect of, 346
Digitoxin, renal excretion, 572
Digoxin in left ventricular failure, 458
— — study of influence of heart rate on heart output, 618
Dihydroergocornine, adrenolytic action, 15
—, circulation and, 268
—, development of tolerance, 60
—, haemodynamic effects in man, 493
— in arrhythmia during cyclopropane anaesthesia, 15
— — essential hypertension, 161
—, intramuscular, cerebral circulation and, 574
—, renal haemodynamic effects, 574
Dihydroergotamine in arrhythmia during cyclopropane anaesthesia, 15
— — normal subjects, 573
Dihydrostreptomycin inhibitors, 461
— in gonorrhoea, 646
— — tuberculosis, 664
—, toxic effects, 578
Dihydroxyphenylbenzyl trimethylammonium dimethylcarbamate, pharmacology, 124
Diisopropyl fluorophosphonate, pharmacological activity, 121
— —, pharmacology, 13
" Dilvasene ", pharmacology, 575
p-Dimethylaminoazobenzene and production of pancreatic tumours in rats, 248
N(2 - Dimethylamino - *n* - propyl) phenothiazine hydrochloride, *see* " Phenergan "
Dimethylethyl - β-hydroxyethyl. ammonium sulphate, dibuty. urethane of, ganglionic block. ing action, 12
3: 4-Dimethyl-5-sulphanilamidoisoxazole, clinical evaluation, 17
Diodone, renal clearance values, 195
Diopterin in pernicious anaemia, 383
— — sarcoma, 577
Dioxycoumatinyl - acetic acid, ethyl ester of, see " Pelentan "
" Diparcol ", anticonvulsant and local analgesic actions, 14
—, basal metabolism and, 346
— in Parkinsonism, 91, 313
—, pharmacology, 14
—, raised metabolic rate and, 313
Diphosgene, inhaled, localization of site of action, 239
Diphtheria antitoxin, concentration in cord blood and rate of loss in babies, 45*
—, bacteriaemia at onset of, 211
— carriers, penicillin in, 322, 544
— —, *x* rays in, 470
— immunity, duration after protamine diphtheria toxoid injection, 99
— immunization in infants, 225, 563
— in newborn, penicillin in, 545
— infection and spread, 226
— paralysis, blood and cerebrospinal fluid in, 211
—, skin factor in Schick reaction, 147
— toxoid, purified, 605
— —, —, protamine and, 477
Diplococcus, non - pathogenic, pathogenic organisms and, 350
" Diplomycin ", clinical trials, 579
Disease, chronic, in old age, 2, 113
— in pre-Hippocratic era, 560*
Disorientation in flight, non-visual stimuli and, 345
Distomiasis, familial epidemic due to *Fasciola hepatica*, 110
Diuresis, activation in jaundice, 638
—, atropine in, 16
—, pitressin and deoxycortone acetate in, 290
—, production by sparteine sulphate, 16
—, water, inhibition by ischaemic muscle pain, 231
Diverticulitis of colon, 30
" Doctor's mob " of 1788, 672*
Dogs, tuberculous infection from, 425
" Dramamine " in air-sickness, 48
— — radiation sickness, 242
— — sea-sickness, 48
Ductus arteriosus, patent, with coarctation of aorta, 247
Dundee, old infirmary of, 1798–1855, 336
Dyestuffs, bladder lesions due to, 116
Dysentery, incidence in England and Wales, 115
— in South Persia, 100
Dysostosis, mandibulo-facial, heredity in, 366
Dyspepsia, gastric secretion and, 503
Dysphagia due to right aortic arch and left ligamentum arteriosum, 473
Dyspnoea of coal-miners, " neoepinine " in, 279
Dystonia, torsion, 311
Dystrophy, adiposogenital, pituitary implantation in, 291
—, dermo-chondro-corneal, familial, 46
—, muscular, electromyography in, 89
—, —, progressive, 314

Eczema, chronic, dermatitis herpetiformis and, 398
—, liver function in, 295
Edinburgh, barber surgeons of, 560*
Elastosis, senile, fibrous changes in dermis, 299
Electric shock therapy, *see* Shock therapy
Electrocardiogram changes after alcohol ingestion, 463
— in anthrasilicosis, 389
— — arterial orthostatic anaemia, 160
— — bronchial asthma, 485
— — cretinism, 264
— — hypertension, 381
— — pneumothorax, 151
—, intracavitary, potential variations in right-sided, 154
—, intravenous tetraethylammonium chloride effect, 154
—, precordial T wave in infants and children, 263
—, Q–T interval in pregnancy, 155
—, reduction in coronary flow and, 154
—, voluntary movement and, 524
Electrocardiograph, semi-direct leads of, 154
Electrocardiography, 154–5
—, low voltage in, cause and effects, 263
Electrocorticography, technique, 524
Electroencephalogram, bilateral prefrontal leucotomy and, 410
—, brain lesions and, 409
—, curare and, 570
— in electric convulsions, 525
— — epilepsy, 524
—, " mesantoin " administration and, 410
—, occipital leucotomy and, 410
— patterns, inheritance in children with behaviour disorders, 88
—, wave and spike complex in, 411
Electroencephalography, 409–11, 524–5
—, hearing loss and, 199
— in cerebral gliomata, 199
— — — tumours, 199
— — spinal-cord disease, 410
—, independent ear electrodes in, 200
— to locate focus of epileptic discharge in Sturge–Weber syndrome, 650
Electrogastrography in gastric carcinoma, 391
Electrokymography, measurement of heart output by, 137
Electrolyte partition in oedema, 33
Electromyogram, interpretation of, 408
Electromyography in lower motor neurone disease, 408
— — muscular dystrophies, 89
Electrothalamogram before thalamotomy in schizophrenia and epilepsy, 88
" Eleudron ", *see* TB I/698 E
Embolism, atheromatous, case reports, 598
—, cerebral, factors affecting prognosis, 527
—, —, stellate ganglion block in, 652
—, peripheral arterial, heparin–papaverine in, 623
—, pulmonary, acute coronary insufficiency due to, 374
Embolus of cotton fibres, pulmonary arteries in, 476
Emotional stress, bladder function disturbances and, 654
Emotions, effect on allergic states, 614, 615
Emphysema, acute mediastinal and subcutaneous, 68
—, chronic pulmonary, 122 cases, 173
—, circulation time and peripheral venous pressure in, 499
—, obstructive, 427
—, pulmonary, respiration and circulation in, 174
—, reserve air as aid in diagnosis, 631
—, respiratory response to carbon dioxide and anoxia in, 629
Empyema, tuberculous, 329
—, —, streptomycin and aspiration in, 551
—, —, TB I/698 therapy, 549
Encephalitis after measles, 528
—, atypical, with glial node formation, 311
— complicating scarlet fever, 99
— in subacute bacterial endocarditis, 202
— lethargica, retarded growth of limbs after, 202
—, post-vaccinal, smallpox vaccination after previous, 563
—, rheumatic, 311
—, Russian Far Eastern, 248
—, subacute inclusion (Dawson type), 311
—, toxic streptomycin causing, 348
—, unrecognized psychotic states after, 415
—, Western equine and St. Louis, diagnosis, 145
Encephalomyelitis, allergic, prevention in guinea-pigs, 93
—, —, production in guinea-pigs, 93
—, disseminated, murine virus causing, 477
—, injection of homologous brain suspensions causing, 93
— virus, equine, local antigenic booster and active cerebral immunity, 45
— —, —, multiplication rate and active cerebral immunity, 44
—, —, Mengo, cultivation, 658
Encephalopathy, test performance in, 532
Endocarditis, 159–60
—, " abacterial ", hitherto undescribed micro-organism in, 144
—, bacterial, in patients over 45 years, 264
—, —, pericarditis in, 156
—, rheumatic and septic, 159
—, streptococcal, penicillin in, 618
—, subacute abacterial, serological findings in, 160
—, — bacterial, 159
—, — —, encephalitis in, 202
—, — —, healed, a new entity, 264
—, — —, penicillin in, 129, 376, 491
—, — —, — and " supronal " in, 159
—, — —, — -treated, morbid anatomy, 159
—, — —, serological classification of *Streptococcus viridans* from, 254
—, — —, streptomycin in, 235
Endocrine disorders, 74–7, 182–5, 290–4, 396–7, 505–8, 640–3
— —, blood formation and, 164
— factors in hypertension, 381
Endocrinology, Thomas Addison, pioneer of, 336*
Endophlebitis hepatica obliterans, 36
Entamoeba, effect of " Win 1011 " and " Win 246 " on, 440
— *histolytica* cysts, ozone water and, 439
Enteric, *see* Typhoid
Enteritis, *Salmonella*, chloramphenicol in, 662
—, *Shigella*, streptomycin in, 423
Enterocolitis, streptomycin in, 551
Enterogastrone concentrates, human gastric secretion and, 69
—, peptic ulcer and, 70
Enzyme inhibitors, proteolytic, in blood, 475
Eosinophil response to sensitization, anaphylaxis, and antihistaminic drugs, 151
Eosinophilia, tropical, adrenocorticotrophin and, 642
Ephedrine in bronchospasm, 279
— — vasoconstriction, 574
Epicatechin and ascorbic acid, capillary fragility and, 497
Epidemiology, 339–40, 450–1, 565–6
Epidermodysplasia verruciformis, generalized verrucosis and, 298
Epilepsy as sequel of recurrent malaria, 529
—, electrical activity of subcortical areas in, 524
—, electroencephalogram in, 525
—, electrothalamography in, 88
—, " epidon " in, 312
—, idiopathic, gestation and, 414
—, latent, barbiturate narcosis in diagnosis, 313
—, minor, " tridione " in, 205
— seizures, syncope and, 205
—, status epilepticus, paraldehyde, 313
Epinephrine, *see* Adrenaline
*nor*Epinephrine as a pressor drug, 233*
" Epituberculosis " in children, 427
Equilibrium disturbances due to streptomycin, 131
Ergometrine maleate, vascular reactions to, 575
Ergosterol, non-irradiated, in calciferol-treated lupus vulgaris, 511
Ergotamine tartrate, action in normal subjects, 573
Erysipelothrix rhusiopathiae infection of mice, sulphanilamide and penicillin in, 188
Erythema induratum, calciferol in, 582
— nodosum in children, 537
— —, radiological appearances of lungs in, 246
Erythermalgia of extremities, 380
Erythroblast hyperplasia, induced, nitrogen mustard and, 170
Erythroblastosis foetalis, exchange transfusion in, 47, 497
— —, osseous changes in, 140
— —, pathogenesis, 497
— —, production in rabbit, 276
Erythrocyte aggregation changes, 382
— in acute hepatitis, 273
— — carcinomatous patients, 249
—, infused, metabolic fate, 465
— sedimentation rate in streptomycin-treated tuberculous meningitis, 433
—, transfused, survival rate, 64
" Etamon ", *see* Tetraethylammonium chloride
État marbré of thalamus after birth injury, 203
Ethyl carbamate, *see* Urethane
— chloride in contact dermatitis, 78
— mercury phosphate in skin mycoses, 78
Ether sign of death, 27
2-Ethyl-3-propyl-glycidamide, 121
Ethylene dicoumarin in disseminated sclerosis, 89
Excitement states, nikethamide and electric shock therapy in, 208
Exercise and curare in anterior poliomyelitis, 210
—, auricular fibrillation and, 57
— in combined degeneration of spinal cord in pernicious anaemia, 412
— — diagnosis of coronary insufficiency, 56
— tolerance in anxiety and relaxation, 533
Extrasystole, systematic physical and psychiatric examination in, 533

Face, keratosis pilaris rubra atrophicans of, 190
Factor V, plasma levels in parenchymatous hepatitis and obstructive jaundice, 252
Faeces in chronic relapsing pancreatitis, 71
—, occult blood in, tests for, 602
Family Service Units for " problem families ", 564
Fasciola hepatica, familial epidemic due to, 110
Fat absorption in coeliac disease, 610
— —, dietary starch and, in coeliac syndrome, 47
—, dietary, importance of, 343
—, —, in aetiology of sprue, 633
— emulsion, intravenous feeding, 568
— metabolism and sprue syndrome, 370
Fatigue, disease and, 485
Felty's syndrome, 306
Fever, *see also* Pyrexia
— therapy in gonococcal arthritis, 85
Fibrillation, *see* Arrhythmia
Fibroblast division, urethane and, 35
Fibrosis, pulmonary, in scleroderma, 399
Fibrositis, fibro-fatty tissue and, 198
Fièvre boutonneuse, chloramphenicol in, 543
Filariasis control by DDT, 135, 136
—, " hetrazan " in, 222, 333, 446
Fingerprint photography, mercury poisoning from, 467
Fleming, David, and ligation of carotid artery, 336*
Flight, Arctic, long-range, physiological responses, 345
Flocculation tests in liver disease, 179
Fluid, body, during protein depletion, choline and, 289
—, extracellular, in obesity, 260
—, —, in thyrotoxicosis, 396
Fluorescent light, burns due to, 227
Fluorine poisoning, dental opacities and, 176
Fly control by DDT spray, 115
Flying, high-altitude, erythrocyte count in, 569
—, —, haemotoxic role of oxygen, 569
Foetus, irradiation injury, 243
Folic acid antagonists and liver extract in pernicious anaemia, 275
— — — in acute leukaemia, 382
— — —, prolonged administration of, 169
— — —, review, 164
— — in megaloblastic anaemia, 275
— — — pernicious anaemia, 383
— —, respiratory and nitrogen metabolism and, 576
— — in sarcoma, 577

Folk medicine, practitioners of, 560*
Food consumption in U.S. army camps, 7
— — of soldiers in subarctic climate, 8
— in sixteenth and seventeenth centuries, 559*
— intake during rest, industrial efficiency and, 566
— proteins, processing and cooking effects, 568
Footwear manufacture, primary irritants and sensitizers used in, 510
Forceps, obstetric, David Davis and history of, 672
" Formocibazol " in infantile diarrhoea, 255
" Fouadin ", *see* Stibophen
Freckles, permanent removal of, 509
Friedreich's ataxia, psychiatric changes and, 315
Fungus poisoning, *see Amanita phalloides*

Galen as a modern, 336
Gall-bladder, biliary constituents in, 454
Galli Mainini reaction for blood stains from pregnancy, 467
Gallop rhythm, *see* Arrhythmia
" Gammexane " in control of *Anopheles gambiae*, 586
" Gantrisan ", clinical evaluation, 17
Gas gangrene, penicillin and streptomycin in, 253
Gastric, *see also* Stomach
— acidity, peptic ulcer and, 286
— —, study by direct estimation of *p*H, 635
— juice in sprue, 178
— secretion and subsequent dyspepsia, follow-up study, 503
— —, carbohydrate metabolism and, 502
— —, enterogastrone concentrates and, 69
— —, histamines and antihistamines, effect of, 177
— —, mecholyl in beeswax and, 285
— — and motility, tetraethylammonium bromide and, 391
— —, nocturnal, in benign gastric ulcer, 71
— —, thiouracil and, 182
Gastritis, chronic, gastric secretion in, 284
—, —, " phenergan " in, 177
—, prepyloric local, 591
Gastro-enteritis, infantile, " benadryl " and sulphamezathine in, 149
—, —, chloramphenicol in, 481
—, —, clinical and bacteriological investigation, 46
—, —, *Staph. pyogenes* and, 481
—, —, streptomycin in, 256
Genetics, 118
Genital glands, 76–7, 184–5
Genito-urinary disorders, 83–4, 195–7, 304–5, 403–4, 517, 647
Germitrine and germitridine, hypotensive action, 573
Giardiasis, " nivaquine " in, 441
von Gierke's disease, muscle biopsy in, 370
de Gimbernat, Antonio, 1734–1816, 224*
Gingivo-stomatitis outbreak in Australian troops in Japan, 3
Glioma, cerebral, electroencephalographic findings in, 199
—, —, radiotherapy, 588
—, —, — at operation, 471
γ Globulin in common cold, 210
Ac-Globulin stability in stored human plasma, 456
Glomerulonephritis, *see* Nephritis, glomerular
Glomerulosclerosis, diabetic, 613
—, intercapillary, in diabetes mellitus, 153
Glossitis and steatorrhoea after ileocolostomy, treatment, 288
— in Addisonian pernicious anaemia, vitamin B complex in, 276
—, nutritional, animal protein factor and, 166
Glucose, blood level, effect on adrenal cortex secretion, 8
—, intestinal absorption, in diagnosis of portal vein obstruction, 390
—, intravenous, effect on beta cells of islets of Langerhans, 359
—, —, cardiac output and, 156
— tolerance in peptic ulcer, 176
— — test, diagnostic value, 74
— — — in liver cirrhosis, 69
Glycosuria, non-diabetic, in chronic schizophrenia, 316
Goitre in African history, 111
—, sporadic, bismuth salt in, 75
Gold poisoning, BAL in, 464
— therapy in rheumatoid arthritis, 407
— — — — —, comparison with copper salts, 85
— — — undulant fever, 439
Gonadotrophin excretion, carcinoma diagnosis by, 249
— in anterior pituitary, cytochemical demonstration, 291
— response, hyper- and hypothyroidism and, 75
Gonococcus, cross-absorption experiments and factor serum determinations, 194
—, thermostability, 194
Gonorrhoea, 193–4, 646
—, aureomycin in, 193, 646
—, chloramphenicol in, 513, 514
—, dihydrostreptomycin in, 646
—, penicillin in, local submucous injection, 646
—, — —, oral, 646
—, — —, prophylaxis by, 193, 300
—, sulphathiazole in, 82
Gothlin test during dicoumarol therapy, 16
Gout, adrenocorticotrophin in, 306, 642
—, heredity, hyperuricaemia and, 371
—, 17-ketosteroid output in, 52
—, liver function and serum protein structure in, 52
—, uric metabolism in, 488
Granuloma annulare, calciferol in, 79
— —, rheumatoid arthritis and, comparative histology, 299
—, cutaneous, beryllium causing, 116
—, eosinophilic, of skin, 644
—, gastric submucosal, 37
— inguinale, aureomycin in, 191, 513
Granulomatosis, pulmonary, chronic, 340
Graphite workers, pneumoconiosis in, 453
Grass-pollen extract, specificity of blocking antibody induced by, 151
Grima, Michel'Angelo, Maltese surgeon of eighteenth century, 112*
Growth disturbances after brain injury, 526
— in rats, xanthopterin and, 66
Guaiacum, the holy wood from the New World, 224*
Guglielmo's disease, 495
Gynaecomastia, aetiology and case reports, 184
Gynaecomastia in paraplegia, 77
—, liver disease and, 638
" Gynergen ", *see* Ergotamine tartrate

Haemagglutination inhibition by thermolabile component of serum, 477
— test for rheumatoid arthritis, 520
Haemangioma of cranial vault, 590
Haematemesis in chronic peptic ulcer, 70
Haematoma, subdural, in infants, 609
Haematopoiesis, endocrine disorders and, 164
—, oestrogens and, 277
—, xanthopterin and, 66
Haematopoietic system, 66, 170–1, 277–8, 384–7
— — in typhus, 321
Haemoglobin concentration and physical fitness, 567
— value during rest and exercise, 455
— — in African children, 496
Haemoglobinuria, nocturnal, case report, 167
—, —, clinical, serological, and therapeutic study, 384
—, —, haemolysis in, 628
—, —, histological study, 168
—, paroxysmal (cold), haemolysis in, 167
Haemolysin in acquired haemolytic anaemia, 276
— — blood incubated at 37° C., 167
Haemolysis in paroxysmal (cold) haemoglobinuria, 167
Haemolytic disease, congenital, due to A-O isoimmunization, 47
— —, —, blood group A and Rh immunization and, 384
— —, —, exchange transfusion treatment, 64
Haemophilia, prothrombin consumption in diagnosis of, 382
Haemorrhage, cerebral, factors affecting prognosis, 527
Haemorrhagic diseases, 168, 497–8
— —, ulcerative, 425
— fever in Bukovina, 259
Haemosiderosis, blood transfusion and, 25
Hair growth, sex hormones and, 76
—, human, phase-contrast microscopy of, 360
— waving by cold-wave process, clinical appraisal, 186
— — — — — —, health and, 462
— — — — — —, optic neuritis from, 462
Hale-White, *Sir* William, 560*
Hallervorden-Spatz disease, 311
Hallucinations, auditory, in schizophrenia, 94
Handkerchief in transfer of respiratory infection, 67
Harvey's role in history of medicine, 224*
Hay-fever, alcohol injection in, 49
Head injury, medico-legal problems of, 467
Headache, adrenaline in, 526
—, forms of, 307
—, frontal, due to aneurysm of intracranial carotid artery, 653
—, histamine in, 200
— in essential hypertension, 269
—, nerves of dura mater in, 200
—, vasomotor, dihydroergotamine in, 620*
Hearing loss, electroencephalographic diagnosis, 199
— of air pilots, 569
Heart, 54–6, 156–8, 264–7, 375–8, 490–3
—, ankylosing spondylitis and, 156
—, atrium, septal defect, chronic cyanosis in, 492
—, —, — —, dynamics of experimental, 119
—, —, volume elastic properties, 119
— block, complete, 58
—, bundle branch block, right, and cardiac infarction, 56
— catheterization in congenital heart disease, 378
— changes in tuberculous children, 247
—, **congenital affections,** 58–9, 492–3
—, — —, catheterization in suspected, 378
—, — —, circulation times in, 59
—, — —, genetics and environment in, 492
—, — —, pulmonary stenosis with closed ventricular septum, 493
—, — —, — —, Potts and Blalock techniques, 58
— disease, blood-gas analysis in, 376
— —, hypertensive and ischaemic, 266
— — in pregnancy, 617
— —, plasma tocopherol levels in, 157
— —, rheumatic, coronary occlusion and myocardial infarction associated with, 619
— enlargement, apparent, in funnel-shaped thorax, 245
— failure, congestive, adaptation of body to, 265
— —, —, definition of cations and anions in, 33
— —, —, dicoumarol in, 347
— —, —, effect of exercise and hypoxaemia in, 375
— —, —, mercurial diuretics and, 617
— —, —, post-operative blood coagulation in, 251
— —, —, salt restriction in, 54
— —, —, theophylline ethylene diamine in, 617
— —, —, " thiomerin " in, 233
— —, left ventricular, digoxin in, 458
— —, — —, pulmonary circulation in, 263
— —, reversible, auricular fibrillation causing, 377*
— injury in experimental hypothermia, 611
—, interatrial septal defect, 266
—, — — —, aberrant insertion of pulmonary veins in, 356
—, interventricular septum, infarction of, 267
—, left auricle, massive dilatation of, 55
—, — ventricle, efficiency in man, 157
— lesions in acute rheumatism, experimental induction, 223
—, mitral stenosis, dicoumarol in repeated embolism in, 158*
—, — —, Lambl's excrescences and, 157
— murmurs due to variations in first apical sound, 490
— — in cardiac aneurysm, 376
— — — coarctation of aorta, 162
—, old age and, 375
— output, adrenaline and, 575
— —, electrokymographic measurement, 137
— —, hypertonic glucose solution to increase, 54, 156
— — in auricular fibrillation, 57
— —, sodium thiocyanate and, 156

Heart pain, triple rhythm in, 378
—, reserve power of, 379
—, ventricular septal defect, 492
— volume, relation to pulse rate and blood volume in exercise, 455
—, *x* rays and, 468
Heat loss in extremities, precooling arterial blood and, 455
— -maintenance function of descending nerve fibres, 454
—, nutritional value of food proteins and, 568
— therapy, intra-articular temperature and, 466
Heberden's nodes, menopause and, 405
Helminth infections, 220–2, 332–3, 444–6
Hemianopia, altitudinal, streptomycin and, 130
Hemiballismus, electrical activity in, 199
Heparin action, protamine and, 459
— co-factor, clinical studies, 274
— in disseminated sclerosis, 200
— — Pitkin menstruum for coronary artery thrombosis, 56
— — rheumatic fever, 446
—, papaverine and, in peripheral arterial embolism, 623
—, prolongation of effects of, 623
—, subcutaneous, prevention of pain by hyaluronidase, 623
— therapy, 584
— tolerance in acute rheumatism, 333
— — test *in vitro* for thromboembolic disease, 251
Hepatitis, acute, erythrocyte diameter in, 273
—, —, transfusions and inoculations in, 504
—, infective, coproporphyrin concentration and isomer distribution in urine in, 39
—, —, deoxycortone acetate in, 658
—, —, effect of alcohol and exertion on liver after, 180
—, —, in children, sequelae, 367
—, —, pathology, 96
—, —, portal cirrhosis and, 181
—, nicotinic acid in, 181
—, parenchymatous, prothrombin and factor-V plasma levels in, 252
—, post-mortem examination in, 639
—, primary, bile flow in, 180
—, viral, electrophoretic studies of serum proteins in, 639
Hepato-lenticular degeneration, *see* Wilson's disease
Hernia, lumbar fatty, 519
Herpes multiplex, smallpox vaccine injections and, 80
— simplex, aureomycin in, 189
— — virus in chick embryo, aureomycin action on, 578
— zoster, aureomycin in, 537
— —, chickenpox and, 209
— —, dehydroergotamine methanesulphonate in, 657
— —, sensory nerves of skin in, 538
— —, vesicle and spinal fluids from, 318
— —, — fluid, cytology, 210
"Hetrazan" in filariasis, 222, 333, 446
— — loiasis, 332, 333
— — onchocerciasis, 333
Hexaethyltetraphosphate, pharmacology, 123
Hicks, John Braxton (1823–1897), 560*
Hirschsprung's disease, colonic peristalsis in, 502
Hirsutism, idiopathic, excretion of 17-ketosteroids in, 397
His, Wilhelm, jr., biography, 112
Histamine, action on hydrochloric acid and pepsin secretion in man, 177
— antagonism with alkyl homologues of ethylamines, 12
— antagonists, "anthisan" and "phenergan" as, comparison, 49
— —, cardio-respiratory effects of, 574
— —, common cold treated by, 539
— —, eosinophilic response to, 151
— —, gastric secretion and, 177
— — in allergic experimental nephritis, 517
— — — bronchial asthma, 369, 486
— — — tuberculosis, 215
— —, "thenfadil", toxic properties, 463
— —, toxicity and side-effects, 615
— headache, desensitization treatment, 200
— in disseminated sclerosis, 308
— — nervous diseases, 651
—, liberation by adrenaline from isolated lung, 574
—, renal function in hypertension and, 160
Histoplasma capsulatum, growth inhibition by tomatin, 209
— —, isolation from soil, 144
Histoplasmosis, clinical, pathological, and mycological observations in, 209
— in children, 109
History of medicine, 111–12, 224, 335–6, 447–8, 599–60, 672
Hodgkin's disease, lymph-node study in, 65
— —, nitrogen mustard in, 171, 278, 387, 625
— —, sternal marrow biopsy in, 66
— —, stomach in, 71
— —, surgical treatment, 387
von Hohenheim, Theophrast, Basle pamphlet on, 336*
Holmes–Adie syndrome, 307
Hormone responses after exposure, 182
Hormones in hyper- and hypotension, 505
—, sexual activity and, 184
Hospital in-patients, elderly male, return to work of, 227
—, military, of Val-de-Grace, 560*
Hunger bradycardia, atropine in, 377
Hunter, John, and his museum, 224*
—, William, early medical education, 560*
—, —, *On the Gravid Uterus*, 559*
Hyaluronidase, absorption of radiopaque substances and, 29
—, heparin injection pain prevented by, 623
— in dehydration of infancy, 366
— — fluid administration, 606
— — localized pretibial myxoedema, 190
— — mucinous infiltration of skin, 190
— of *Streptococcus haemolyticus* group A, inhibitor in human serum, 362
Hydrocephalus, congenital, stenosis of Sylvian aqueduct causing, 257
Hydrochloric acid secretion, histamine and, 177
4-Hydroxycoumarin, prothrombin time and, 576
Hydroxystilbamidine in kala-azar, 332
Hygiene, 1–6, 113–17, 225–8, 337–41, 449–53, 561–6
Hyperhidrosis, radiotherapy, 81
Hyperostosis, congenital diffuse generalized, 37
Hyperparathyroidism, *see* Parathyrotoxicosis
Hyperpyrexia, therapeutic, pathology of fatal cases, 476
Hypersensitivity, horse serum in rabbits and, 33
Hypertension, 269–71, 380–1
—, arterial, adrenal cortex and, 270
—, —, urinary stasis and development of, 161
—, autonomic nervous system in, 270
—, cardiovascular, in bilaterally nephrectomized dogs, 380
—, cerebral circulation, bilateral stellate ganglion block and, 160
—, chronic, mechanism of vicious circle in, 621
—, compound E in, 135
—, electrocardiogram in, 381
—, essential, blood and bone marrow in, 624
—, —, contemporary views on, 161
—, —, lumbar puncture and, 269
—, —, medical and surgical treatment, comparison, 269
—, —, protein deficiency and blood pressure in, 622
—, —, psychiatric factors in, 415
—, —, sympathectomy and, 59
—, —, veratrum viride and dihydroergocornine in, 161
—, histamine and renal function in, 160
—, ischaemic heart disease compared with, 266
—, menopausal, 270
—, minimal sodium diet and blood pressure in, 380
—, oxygen in, 60
—, pentamethonium iodide in, 271
—, prefrontal leucotomy for, 622
—, prolonged interrupted narcosis in, 269
—, renal arteries, compression of, causing, 59
—, renin in blood in, 381
—, retinal vessels in, 271
—, salt-active corticoids in, 60
—, sympathectomy, 621
—, —, follow-up, 160
—, —, high dorsolumbar, 60
—, tetraethylammonium bromide in, 379
—, thiocyanate in, 620
—, vitamin A in, 270
—, *x*-irradiation of pituitary and adrenal regions in, 381
Hyperthyroidism, *see* Thyrotoxicosis
Hyperventilation syndrome, 315
Hypoglycaemia, functional, in children, adrenocorticotrophin in, 290
—, spontaneous, 51
—, thrombo-angiitis obliterans treated by, 375
Hypoparathyroidism, pseudo-, with late manifestations, 293
Hypophysis, *see* Pituitary
Hypopituitarism, *see* Pituitary deficiency
Hypopotassaemia, development during therapy of diabetic acidosis, 53
Hypoproteinaemia, nephrogenic, plasma transfusions and, 84
Hypotension, deoxycortone acetate and sodium chloride in, 76
—, haemorrhagic, morphine in, 10
—, sex hormones in, 505
Hypothyroidism, *see* Myxoedema; Thyroid deficiency
Hypoxia, *see* Oxygen deficiency
Hysteria, prognosis of certain symptoms of, 207
Hysterosalpingography, absorption of radiopaque substances used in, 594
—, sources of functional disturbance in, 141
—, water- and oil-soluble contrast media, 593

Ichthyosis, vitamin A and choline in, 644
Icterus, *see* Jaundice
Immunity, 44–5, 145–7
— of mice infected with *Ascaris lumbricoides* larvae, 222
Impetigo, bacitracin in, 188
Industrial medicine, 6, 115–17, 226–8, 340–1, 451–3, 566
— —, history, 560*
— —, Paracelsus and, 560*
Infant, congenital anomalies, recurrence in siblings, 118
—, — malformations, maternal conditions and, 480
— feeding, difficulties in, 365
— —, wheat germ in, 46
— mortality in Czechoslovakia, 480
—, newborn, new syndrome of, 258
Infarcts, cerebral and retinal vascular occlusion and, 33
Infections, air-borne, in isolation wards, 226
— in children, nutrition and, 148
—, neonatal, incidence, 481
Infectious diseases, 95–110, 209–23, 318–34, 417–46, 537–8, 656–71
— —, acute, precipitation of endogenous psychoses by, 94
Influenza, aureomycin in, 632
— immunity, passive, in infants, 478
— infection in mice, 253
— in Highlands of Scotland, 565
— — Sweden, 114
— -like diseases, differential diagnosis, 417
Injection, intraneural, fate of, 9
Insecticides and repellents, 135–6, 586
— — —, "kik", activity of, 586
Insulin allergy and resistance, 613
—, chemical combination with muscle (diaphragm) of rat, 373
—, — — — —, hormonal influences on, 261
— coma, blood transfusion in, 489
— —, prolonged, potassium in, 317
— discovery, history, 112
—, hyperglycaemia – glycogenolytic factor in, 372
— hypersensitivity in pellagra, 488
— in schizophrenia, follow-up, 208
—, modified protamine, clinical report, 372
— "NPH-50", clinical report, 372
—, —, — trial, 52, 53
—, protamine-zinc, retarded absorption of, 261
— shock therapy in women, 536
—, skin reactions to, 612
— test for vagal secretion, 637
— tolerance test in liver cirrhosis, 69
Intelligence, juvenile delinquency and, 26
Intestinal tract operations, macrocytic anaemia and, 166
Intestines, 178–9, 288, 393–4
—, obstruction, congenital, due to errors of rotation of midgut, 607
—, perfusion, hypotonic solutions in, 304

Intestines, small, radiology in old age, 31
—, stricture and anastomosis, macrocytic anaemia with, 166
" Intocostrin " in spastic paralysis in children, 650
Intussusception, acute, in angioneurotic oedema, 608
—, —, in infants and children, 607
—, recurrent, of small intestine in children, 608
Iodides, effect of administration with thiouracil, 640
Iodine, organic binding by thyroid, effects of thiocyanate and thyrotropin on, 293
—, radioactive, in measurement of thyroid function, 396
—, —, — metastatic thyroid carcinoma, 588
—, —, — thyrotoxicosis, 507–8
—, —, protein-bound, in diagnosis of hyperthyroidism, 74
—, —, rate of conversion into protein-bound iodine of plasma in evaluating thyroid function, 397
—, —, thyroid collection in senescence, hypothyroidism, and hypopituitarism, 74
—, —, urinary excretion in diagnosis of thyroid disorders, 396, 397
— utilization by thyroid, effect of iodide ion on, 506
— values in blood, microdetermination, 567
Iodocasein, radioactive, in myxoedema, 291
Iodophthalein elimination as test of liver function, 40
Iodothiouracil in thyrotoxicosis, 293
" Ioduron B ", bronchography with, 590
Iontophoresis in peripheral vascular disease, 271
Ipecacuanha in gastric radiography, 141
Iron deficiency without anaemia, 612
—, intravenous, in anaemia of pregnancy, 63
—, —, in hypochromic anaemia, 625
—, radioactive, intravenous, utilization in iron metabolism, 274
— –sucrose preparation, intravenous, in anaemia, 62
— therapy, digestive disturbances during, 496
— —, effect on serum iron level, 496
Irradiation injuries of skin, tubercle-like structures in, 29
—, ionizing, haemorrhagic disease caused by total-body exposure to, 587
—, micro-wave, effect on animals, 585
—, total body, tissue changes in, 469
Ischaemia of renal cortex, anuria after, 84
" Isuprel " analogues, bronchodilator activity, 346
" Itchy skin ", tetraethylammonium chloride in, 189

Jarisch – Herxheimer reaction following penicillin therapy, 191
Jaundice, artificial, in Parkinsonism and disseminated sclerosis, 309
—, differential diagnosis, bile flow in primary hepatitis and, 180
—, — —, single serum sample analysis in, 360
Jaundice, diuresis in, 638
—, epidemic, isolation of virus in, 319
—, familial haemolytic, haemolytic crisis in, 167
—, homologous serum, 419
— in syphilis, 401
—, obstructive, coproporphyrin concentration and isomer distribution in urine in, 39
—, —, prothrombin and factor-V plasma levels in, 252
Jejunum dilatation, 590
Jenner, Edward, and his work, 560*
Joint function, rheumatoid arthritis and, 85
— lesions produced by deoxycortone acetate, 293
Jones, Anson, doctor and diplomat, 672*
Jurisprudence, medical, 467

Kala-azar, hydroxystilbamidine in, 332
—, indigenous, in Gambia, 556
Kaolin, effect on lungs of rats, 6
Kaposi's disease, diabetes mellitus and, 644
— varicelliform eruption, aureomycin in, 189
— — — due to vaccinia virus, 78
Keratosis pilaris rubra atrophicans of face, 190
Ketene, air-borne, physiological response to, 240
Ketone metabolism in health and liver disease, 504*
Ketosis, diabetic, electrolyte balance in, 613
Ketosteroid excretion, convulsion therapy and, 536
— — in heat and cold stress, 182
—, urinary excretion in gout, 52
—, — — — idiopathic hirsutism, 397
—, — —, testosterone treatment and, 77
—, — —, values in relation to age and sex, 76
Khellin, *see* Visammin
Khirov Academy of Military Medicine, 150 years of obstetrics and gynaecology at, 224*
Kidney, *see also* Nephritis, etc.
—, anoxic anoxia and, 196
—, artificial, clinical experiences with, 197
—, —, in uraemia, 83
—, —, potassium in dialysing fluid in treatment with, 83
— atrophy, bilateral focal ischaemic, 599
— biopsy in renal tumours, 403
— blood flow and clearance, partial obstruction of renal vein in, 36
— carcinoma, 304
— circulation, experimental studies and clinical aspects, 517
— —, history of research on, 559*
— —, neurovascular control of, 517
— clearance tests, difference in systemic arterial and venous plasma concentrations in, 195
—, congenital polycystic disease, 403
— cortex, anuria after ischaemia of, 84
— disease, blood and bone-marrow studies, 624
— —, renal clearance and excretion index in, 305
— —, rice diet in, 494
— failure and low extracellular sodium chloride, 305
— — from lysed erythrocytes, 196
Kidney function, benzoic acid and caronamide and, 129
— — in congestive heart failure, 617
— — — hypertension, 160
— — — myxoedema, 182
— — — Rocky Mountain spotted fever, 540
— —, increased renal venous pressure and, 36
— haemodynamics, water deprivation and, 120
— hypertrophy after nephrectomy, thyroid gland and, 75
— lesions, choline deficiency producing, 596
— — in diabetes mellitus, 403
—, plasma flow, clearance method of determination with diodone, *p*-acetylamino-hippuric acid, and *p*-amino-hippuric acid, 250
—, potassium deficiency production and, 403
— regulation of acid–base balance in man, 120
— response to hypertonic solutions of sodium chloride and urea, 231
—, sodium excretion, adrenal cortex and, 343
—, tetraethylammonium bromide and, 123
—, toxic effect of bacitracin on, 349
— tuberculosis, pulmonary and urogenital tuberculosis in pathogenesis, 435
— tumour, diagnosis by renal cytogram, 403
—, vascular " shunt ", experimental demonstration, 517
" Kik ", activity of, 586
Klare's scheme and course of pulmonary tuberculosis, 553
Kleptomania in males, 654
Knee-joint, opaque arthrography of, 141
Knipping–Scoz test in silicosis, 117
Kravkov, Nikolai Pavlovich, Soviet pharmacologist, 224*
Kveim reaction in sarcoidosis, 387
Kwashiorkor, therapeutic studies, 487

Lambl's excrescences, mitral valve stenosis and, 157
Larynx, tuberculosis of, TB 1/698 E treatment, 549
Laterosporin A and B, 18
Laxative, sodium carboxymethylcellulose as, 394
Lead poisoning, BAL in, 240
— — in pottery industry, 239
— worker, care of, 226
Lebert, H., 1813–78, bibliography, 448*
L.E.-cell phenomenon, production *in vitro*, 273
Left-handedness, brain injury and, 91
Leprosy, lepromatous, 4,4′-diaminodiphenyl sulphone in, 659
—, primary lesion, surgical treatment, 659
—, Russian specialist, Grigorii Nikolaevich Minkh, 560*
—, tuberculoid, vitamin D and " promanide " in, 543
Leptospirosis icterohaemorrhagica in north-east Scotland, 340
Leucocyte count as indicator of drug agranulocytosis, failure of, 40
— — in streptomycin-treated tuberculous meningitis, 433
— level in blood in inflammation, 595
—, lysis by tuberculoprotein, role of complement in, 363
Leucocyte movements, modification by chemicals, 229
Leucocytosis, thermostable component in, 595
Leucosis, experimental, induction by carcinogens, 475
Leucotomy, bilateral prefrontal, electroence phalographic changes after, 410
—, occipital, electroencephalographic changes after, 410
—, prefrontal, clinical and psychological studies in, 535
—, —, in hypertension, 622
—, —, — schizophrenia, 534
—, relapse after, 208
Leukaemia, 168–9
—, acute, aminopterin treatment, 608, 624
—, —, — —, macrocytic erythrocyte development during, 169
—, —, exchange transfusion in, 624
—, —, folic acid antagonists in, 382
—, —, spontaneous remission complicated by eclampsia, 168
—, atypical myeloid, 169
—, blood coagulation in, 360
—, chronic lymphatic, radioactive phosphorus in, 169
—, — myeloid, urethane in, 169
— in negroes, 382
—, monocytic, aminopterin in, 275
—, multiple myeloma as form of, 385
—, radioactive arsenic in, 385
—, serum proteins in, 62
—, stomach involvement, 71
—, *x* rays and urethane in, 30
Leukergy production by tuberculin as test of tuberculosis activity, 363
Lewandowsky's rosacea-like eruption, 512
Lichen planus, calciferol in, 79
Ligamentum flavum, 599
Lipocalcinogranulomatosis, 171
Lipoid metabolism disturbance in atherosclerosis, 619
Lipoma of gastro-intestinal tract, 592
" Lissephen ", *see* " Myanesin "
Listerellosis, angino-septicaemic form, 546
Listeria infection in man, 324
Lithiasis, active broncho-pulmonary, 162
Lithium chloride, substitute for sodium chloride in diet, 581
— periodate, effect on crystalline bovine serum albumin, 41
Little's disease, " parpanit " in, 530
Liver, 179–81, 289, 394–5, 504, 638–9. *See also* Hepatitis
— biopsy for enlarged hilar and mediastinal lymph nodes, 600
— changes during protein depletion, effect of choline on, 289
—, cholesterol deposition in, pancreatic lipotropic factor and, 249
— cirrhosis with ascites, sodium restriction and, 504
— —, blood and bone-marrow appearance in, 164
— —, clinical and histological changes, 394
— —, definition of cations and anions in, 33
— —, electrophoretic studies of serum proteins in, 639
— —, glucose, insulin, and adrenaline tolerance tests in, 69
— —, gynaecomastia and, 638
— —, human serum albumin in, 394
— —, infective hepatitis and, 181

Liver cirrhosis, intravenous amino-acids in, 395
— —, — liver extract in, 394
— —, malnutrition as cause, 638
— —, mercurial diuretics, human serum albumin, and low sodium diet in, 395
— —, serum proteins in, 289
— damage after thiouracil treatment of thyrotoxicosis, 506
— — due to alcohol or sugar, prevention by choline, 595
— disease, central nervous system in, 308
— —, flocculation tests in, 179
— —, methionine metabolism in, 639
— —, nutritional, 179
— —, thrombocytopenia and increased capillary fragility in, 168
—, endophlebitis obliterans, 36
— extract and folic acid antagonists in pernicious anaemia, 275
— — in subacute combined degeneration of spinal cord, 525
—, fatty disease of, pancreatic atrophy in infants with, 150
—, — infiltration, action of pancreatic lipotropic factor on, 248
—, — —, choline in, serial biopsies during, 394
— function, adrenaline-induced hyperglycaemia as index of, 39
— —, colloidal red test as index of, 39
— —, glycogen storage as index of, 39
— — in carbohydrate metabolism, 372
— — — Darier's disease and pityriasis rubra pilaris, 80
— — — gout, 52
— — — Rocky Mountain spotted fever, 540
— — — skin diseases, 295
— —, iodophthalein elimination as test of, 40
— — test using buffered colloidal solutions of benzoin or shellac, 250
— in alcoholism, needle biopsy of, 638
— — migraine, 206
— injury due to diet in rats, 180
—, puncture biopsy in miliary tuberculosis, 429
—, tuberculous foci in, 246
Lobelline, determination of circulation time with, 616
Locomotor system disorders, 85–7, 198, 306, 405–7, 518–23, 648–9
Loeffler's syndrome, adrenocorticotrophin and, 642
— —, case report, 68
— —, relation of disseminated focal necrosis with eosinophilia and arteritis in asthma, 50
Loiasis, " hetrazan " in, 332, 333
Louping-ill, isolation of virus, 95
— meningo - encephalitis, serological survey, 418
Louse infestation of children's heads, insecticides for, 136
" Lucite " plombage in extrapleural pneumonolysis in pulmonary tuberculosis, 553
Lung abscess, penicillin in, 389
—, adenomatosis of, 68
—, ankylosing spondylitis effects in, 198
—, arterio-venous aneurysm of, 67, 356
—, blood vessels in aortic coarctation, 247
— carcinoma, alveolar-cell, 68
— —, increase in deaths attributed to, 338
— —, occupation and tobacco in, 632
— —, pathology, 282
Lung carcinoma, superior vena cava obstruction in primary, 389
— carcinomatosis, diffuse, pathology of subacute cor pulmonale in, 142
— cavitation, bacterial resistance to streptomycin and, 104
— —, tuberculous, spontaneous healing, 669
— disease, calculus formation and, 67
—, miners', Osler on, 224*
— fibrosis due to *Oxyuris vermicularis*, 630
— — in scleroderma, 399
— —, respiration and circulation in, 174
—, function of, in silicosis, 452
— hilar shadows in silicosis, 357
— hilum, acute infiltration of, 664
— **infections,** 631–2
— —, segmental, 389
—, striation-shadows radiating in upper lobe, 139
— suppuration, penicillin in, 173, 279
—, tuberculosis of, *see* Tuberculosis, pulmonary
— **tumours,** 632
— —, alveolar-celled, 175
— —, nitrogen mustard in, 171
— ventilation, alveolar and bronchial factors in, 457
— —, uneven in disease, 630
— volume, pharmacological variations in health, 11
Lupus carcinoma, 510
— erythematosus, acute, 297
— —, chronic, peripheral blood flow in, 511
— — discoides, " mapharside " in, 80
— —, disseminated, adrenocorticotrophin in, 511
— —, —, production of L.E.-cell phenomenon, 273
— —, malignant, 80
— vulgaris, calciferol treatment, 511
— —, — —, polyneuritis complicating, 644
— —, radiotherapy, after-effects of, 510
" Luotest ", testing in late syphilis with, 401
Lymphadenitis, tuberculous cervical, radiotherapy in, 215
Lymph node aspiration in radiotherapy, 244
— — diseases, nitrogen mustard in, 65
— —, enlarged, liver biopsy causing, 600
— — in Hodgkin's disease, tissue culture studies of, 65
Lymphocytosis, infectious, epidemic in children, 606
Lymphogranuloma venereum, bubonic form, aureomycin in, 191
— —, children born of mothers with, 402
— —, laboratory diagnosis, 600
— — virus, resistance in mice due to *Encephalitozoon cuniculi*, 603
Lymphogranulomatosis, benign, *see* Sarcoidosis
Lymphoma, follicular, sternal marrow biopsy in, 66
Lymphosarcoma, nitrogen mustard in, 625
—, sternal marrow biopsy in, 66
Lysergic acid, clinical effects, 463

Macrocheilitis, granulomatous, 190
Magnesium phosphate, adsorbent complex in peptic ulcer therapy, 176
Majocchi's disease and related conditions, 398
Malaria, 107–9, 441–4, 557–8, 669–71. *See also Plasmodium*
—, antibiotic from butterfly-wing extract in, 219
—, " chloroquine ", " pentaquine ", and " neo-premaline " in suppression of, 219
—, — and proguanil in, 670
— control in Venezuela, 339
— eradication, DDT and " gammexane " in, 586
— — in Cyprus, 563
—, falciparum, acute, blood examination in, 330
—, —, antagonism of a bacterial intoxication to, 107
—, —, chloroquine in, 444
—, —, parasite rate at high altitudes, 441
—, —, proguanil-resistant, 669
—, gallinaceum, quinine in, spleen and, 331
— immunity in Africans, 107
— —, development of collective, 219
— in Germany, 1945–7, 107
—, proguanil and prophylaxis in Indo-China, 108
—, recurrent, epilepsy as sequela of, 529
— splenomegaly, chloroquine diphosphate and, 331
—, sulphonamides in, 107
—, synthetic diaminopterins and, 670
—, tertian, benign, long-term latency in, 442
—, —, malignant, treatment, 442
—, vivax, recurrent, status of immunity following cure, 443
Malnutrition, *see* Nutrition deficiency
Mammary carcinoma in mice, isolation of virus, 596
— — — —, survival of milk factor in, 35
— gland, lobular-alveolar development in rat, 290
— — tumour agent in hybrid mice, 34
— — —, hormone responses on transplantation, 35
— tumours, functional differentiation, 598
Manassein, V. A., Russian specialist in tuberculosis, 336*
" Mapharside ", *see* Oxophenarsine hydrochloride
Marasmus, protein requirements of infants in, 606
Marchiafava–Micheli disease, *see* Haemoglobinuria, nocturnal
" Marcus Gunn phenomenon, inverted ", 89
Marfan's syndrome, *see* Arachnodactyly
Marín-Amat syndrome, 89
Measles encephalitis, 528
Mecholyl in beeswax, effect on gastric secretion, 285
—, ulcer production by, 285
Mediastinum, anterior, radiological demonstration in children, 590
— displacement in asthma, 614
— tumour and aneurysm, angiocardiography, 357
Medical education in Scotland, 335
— **jurisprudence,** 26–7
Medicine, eighteenth - century, in Roxburghshire, 224*
—, advance in, in the 1840's, 448*
—, **general,** 48–53, 151–3, 259–62, 368–73, 485–9, 611–15
Mediterranean anaemia, *see* Anaemia, Cooley's
Medulloblastoma, radiotherapy in, 470
Megakaryocyte, pseudo-thrombocyte formation from, 164
Melanoma growth, effect of aminopterin on, 248
—, malignant, bone metastasis in, 358
—, —, surgical and irradiation treatment, 243
—, melanin causing, 595
—, mitochondria and, 229
Melanosis, neuro-cutaneous, 509
Melioidosis, 100
Meningioma, intraspinal, calcification in, 245
—, posterior fossa, 528
—, spinal, myelography in, 140
Meningitis, aseptic, of new virus origin, 540
—, *Bact. coli*, streptomycin in, 202
—, *H. influenzae*, streptomycin in, 484
—, — —, — and penicillin in, 99, 324
—, intestinal organisms causing, streptomycin in, 149
—, *Klebsiella*, streptomycin in, 22*
—, pneumococcal, penicillin in, 428
—, serous, acute, complicating scarlet fever, 99
—, tuberculous, new sign in, 88
—, —, reactive autonomy of leptomeninges in, 329
—, —, streptomycin in, 104, 431, 606, 666
—, —, — —, cerebrospinal fluid changes during, 432
—, —, — —, " promizole " and, 217
—, —, —, " promin ", and vitamin A in, 432
—, —, — treated, allergy and immunity tests in, 433
—, —, TB 1/698 and TB IV effects, 549
—, —, transplacental streptomycin in, 431
—, —, tuberculomata of brain and, 329
Meningo - pneumotrophic virus, relation to psittacosis-like virus, 95
Menopause, blood pressure in, 270
—, Heberden's nodes and, 405
Menstruation, blood clot retraction estimation in, 7
Mental deficiency problems in Great Britain since 1906, 337
— disease, Pinel's conception of, 447
— disturbances in the elderly, 207
Mepacrine, effect on Chesson strain of *Plasmodium vivax*, 443
Mepyramine maleate, *see* " Anthisan "
Mercaptomerin sodium, *see* " Thiomerin "
Mercuric cyanide in syphilitic aortitis, 401
Mercury diuretics, circulatory effects in congestive heart failure, 617
— poisoning, BAL in, 464
— —, chronic, and hyperthyroidism, 23
— — from fingerprint photography, 467
" Mesantoin ", electroencephalographic changes and, 410
Metabolic disorders, 50–2, 152–3, 260–1, 370–1, 486–9
" Methadone ", *see* " Physeptone "
Methaemoglobinaemia, congenital, 495
Methaphenilene hydrochloride, *see* " Diatrin "
" Methedrine " shock in personality exploration, 317
Methionine metabolism in liver disease, 639

N-Methylberbamine, curariform activity, 346
Methyl-*bis* (β-chlorethyl) amine, *see* Nitrogen mustard
Methylcellulose in bowel function improvement, 393
N-Methylisotetrandine, curariform activity, 346
Methyl methacrylate, *see* "Lucite"
Methylphenylethyl hydantoin, *see* "Mesantoin"
Methyl salicylate poisoning, 133
— testosterone administration in rabbit, 76
Microbiology, 41–5, 144–7, 253–4, 362–4, 477–8, 603–5
Microscopy, phase-contrast, and metal-shadowing in study of blood cells, 164
—, —, in morbid histology, 360
—, —, of human hair, 360
Micturition disorders, *see also* Anuria
— — in poliomyelitis, 319
Migraine, personality studies in, 532
—, retinal arterial occlusion in, 531
—, role of liver in, 206
Military surgery in sixteenth century, 112*
Milk, fat content, diurnal variation in, 255
— intake, prolonged, calcinosis after, 51
—, penicillin excretion in, 20
— secretion in the rat, 290
Minkh, Grigorii Nikolaevich, Russian leprologist, 560*
Mitochondria, cloudy swelling and, 247
Mongolism and heredity, 609
Mononucleosis, infective, electrocardiographic changes in, 673
—, —, radiological manifestations, 472
—, —, serum proteins in, electrophoretic analysis, 62
—, —, urine appearance in, 39
Morbid anatomy, 36–7
Morphine, antagonism by 5-amino-acridine, 570
—, gastric radiography and, 141
— and "physeptone" analgesia compared, 10
— —secretin test of pancreatic function, 283
—, vasodepressor responses after haemorrhagic shock, 10
Mosquito eradication in Cyprus, 563
— infected with *Plasmodium gallinaceum*, antimalarial drugs and, 108
— in London, 449
— sounds recorded, field tests in mosquito destruction, 444
Moth balls, acute haemolytic anaemia due to, 353
Motion sickness, air, "dramamine" in, 48
— —, sea, "dramamine" in, 48
Motor neurone disease, electromyography, 408
Mouth ulcers, aureomycin in, 390
Movement, cortico-spinal and subcortico-spinal mechanisms in origin of, 231
Mumps meningo-encephalitis, complement-fixation tests in, 418
— — without parotitis, 418
—, neurological complications, 318
— orchitis, diethylstilboestrol in, 318
—, serological diagnosis, 147
—, specific serological reactions, 605
—, virus isolation and serological studies in, 418
Muscle action potential, duration and form in human, 9
— atrophy, progressive, colchicine in, 412
— biopsy in von Gierke's disease, 370
— dystrophy, progressive, 650
— spasm in rheumatic disorders, curare in, 405
Myalgia, epidemic, 649
"Myanesin" in cerebral palsy, 483
—, effect on experimental spasticity, 576
—, — — motor system, 575
—, — — nervous system, 233
—, summary of recent work, 122
Myasthenia gravis, neuromuscular function in, 412
— —, tetraethyl pyrophosphate in, 122
—, plasma neostigmine levels and cholinesterase inhibition in, 11
Mycobacterium tuberculosis, antagonism of a non-pathogenic diplococcus to, 350
— —, labelling with radioactive phosphorus, 427
— —, morphology and streptomycin effect, 43
— —, murine, vaccination with, 3
— —, neomycin activity, 329
— — resistance to sodium *p*-aminosalicylic acid, 126
— —, slide culture method of examination, 254
— —, streptomycin resistance, persistence *in vivo* and *in vitro*, 552
— —, — —, prevention of, 103
— —, — resistant, relation of cavity to development in pulmonary tuberculosis, 104, 433
— —, — — strains, factors influencing emergence of, 104
Mycokeratosis, palmar and plantar, with onychomycosis, 79
Mycosis fungoides, antimonials in, 512
— —, nitrogen mustard in, 81, 399
Mycotorula albicans, palmar and plantar mycokeratosis with onychomycosis due to, 79
Myeloma, multiple, antimony in, 385
—, —, as form of leukaemia, 385
—, —, Bence-Jones protein of, 171
—, —, clinical report, 386
—, —, urethane in, 170
Myelopathy, transverse, in achondroplasia, 203
Myelosclerosis, subacute, 384
Myelosis, chronic non-leukaemic, 384
Myocarditis, serum-induced, "benadryl" and "neoantergan" in, 122
Myocardium contractility, loss after coronary artery occlusion, 378
— disturbances in infective mononucleosis, 367
— infarction, auricular flutter and, 57
— —, blood transfusion in, 619
— —, chronic rheumatic heart disease and, 619
— —, coronary circulation in, 619
— —, follow-up study, 378
— —, pitressin in, fatal effect of, 158
— —, plasma and blood infusion following, 158
— ischaemia, concepts of, 491
"Myoidema", historical survey and clinical observations, 368
Myxoedema conscriptum thyrotoxicum, 292
Myxoedema diagnosis, 396, 397
—, localized pretibial, hyaluronidase in, 190
—, psychosis and, 292
—, radioactive iodocasein effect in, 291
—, renal function in, 182
—, thyroxine in, 641

Naevus flammeus, post-traumatic, 298
Nails, fungus infections of, 187
Naphthalene poisoning, acute haemolytic anaemia due to, 353
Narco-analysis in personality exploration, 317
Narco-epileptic attacks, mechanism, 206
Narcosis, prolonged, in peptic ulcer treatment, 392
—, — interrupted, in hypertension, 269
Nasopharynx, bacterial flora of, 603
Naval medicine in nineteenth century, 448
Necrosis, disseminated focal, with eosinophilia and arteritis in asthma, 50
"Neoantergen", approved name: mepyramine
—, serum-induced myocarditis and, 122
Neoarsphenamine in syphilis, 514
"Neo-epinine", *see* "Aleudrine"
"Neohetramine" in allergic disorders, 49
— — common cold, 658
— — tuberculosis, 215
"Neo-iopax", pyelography by rapid injection, 246
Neomycin, action on *Myco. tuberculosis*, 329
—, activity *in vivo*, 237
"Neo-premaline" in malaria, 219
Neostigmine, blood level of, and cholinesterase inhibition in dogs and myasthenic patients, 11
"Neosynephrin" in bronchospasm relief, 279
Nephritis, blood and bone-marrow in, 624
—, experimental allergic, antihistamine agents and, 517
—, glomerular, acute diffuse, 404
—, —, —, epidemic, 84
—, —, —, pathogenesis, 305
—, —, renal manifestations of, 195
—, history of, 560*
—, mercurial, prolonged forms of, 84
"Nephrography", experimental and clinical observations, 471
Nephron, structure of metabolic process in, 84
Nephrosclerosis, deoxycortone acetate in, 83
Nephrosis, arterial hypertension and, 161
—, erythrolytic, 37
—, human serum albumin injections in, 195
Nerve(s), acoustic, tumours, radiological manifestations, 471
—, basal ganglions, "panparnit" in diseases of, 651
— block, bilateral stellate ganglion, cerebral circulation and, 160
— conduction, acetylcholine in, 12
—, cutaneous, calibre of fibres in, 455
— fibres, descending, heat maintenance functions of, 454
—, injections into, radioactive phosphorus tracer, 9
Nerve, peripheral, 528–9
—, —, excitability, influence of hypothyroidism on, 75
—, —, injuries from penicillin administration, 129
—, —, smallpox vaccination and, 529
— physiology, quaternary ammonium and sodium ions in, 13
— roots, meningeal spinal, 528
— section, *see* Sympathectomy; Vagotomy
—, stellate ganglion block, in cerebral thrombosis and embolism, 652
Nervous system, autonomic, in hypertension, 270
— —, **central,** 89–91, 200–4 307–9, 411–12, 525–6
— —, —, curare and, 458
— —, —, in liver disease, 308
— —, arsphenamine administration, damage after, 308
— — disease, motor signs, 231
— — lesions, linear scleroderma and, 190
— —, **peripheral,** 204–5
— —, sympathetic, effect of stimulation on auricular flutter, 158
— —, —, involvement in acute poliomyelitis, 96
Neuritis, optic, from cold permanent wave, 462
—, pressure, of deep palmar branch of ulnar nerve, occupational origin of, 89
Neurodermatitis, phenindamine in, 297
Neurology, 88–93, 199–206, 307–14, 408–14, 524–31, 650–3
Neuropathology, historical sketch, 672*
Neurosyphilis, penicillin in, 400, 516
—, — —, follow-up study, 192
—, — and fever therapy in, 400
—, — —, malaria therapy, 645
Neutropenia, chronic, splenectomy in, 170
Nicotinamide in bromide intoxication, 583
Nicotinic acid in hepatitis, 181
Nikethamide and electric shock therapy in states of excitement, 208
— injection in newborn, syndrome following, 258
Nisin, recent applications of, 236
Nitric acid fumes, fatal inhalation of, 232
Nitriles, basic, antispasmodic action, 126
Nitrogen balance in chronic peptic ulcer, 286
— —, raw or heated egg white as dietary protein, 568
— metabolism, folic acid and, 576
— — in chronic idiopathic ulcerative colitis, 288
— mustard analogues in carcinoma, 577
— —, chemical structure and toxicity and pathological effects, 577
— —, effect on regenerating rat liver, 578
— — in bronchial carcinoma, 38
— — — chronic gastric ulcer, 636
— — — glomerulonephritis, 195
— — — Hodgkin's disease, 278, 387
— — — induced erythroblastic hyperplasia, 170
— — — lymph-node diseases, 65
— — — malignant disease, 127
— — — — lymphogranuloma, 625
— — — mycosis fungoides, 81, 399
— — — pulmonary tuberculosis, 16

Nitrogen mustard in reticuloses and pulmonary neoplasm, 171
— — — sarcoma, 578
— —, intraperitoneal, testicular lesions after, 578
— —, necrotizing tonsillitis due to, 22
" Nivaquine ", *see* Chloroquine
Nocardia extracts, tuberculostatic action in white mice, 43
Nocardiosis, case reports, 417, 656
Noradrenaline, circulation and, 460
—, liberation from suprarenal gland, 183
—, optical isomers, acute toxicity, 12
—, vaso- and bronchomotor action in isolated perfused lungs of dog, 121
" Novocain ", *see* Procaine
NPH 50, clinical trial, 52, 53
" NU-445 ", clinical evaluation, 17
" NU-683 ", pharmacology, 124
" NU-2017 ", effects on neuromuscular function, 460
—, pharmacology, 460
" NU-2206 ", clinical trials, 572
Nuclear fission, metabolism of radioactive elements created by, 28
Nurses, health in hospital, 449
Nutrition deficiency as cause of liver cirrhosis, 638
— — diseases and sequelae in concentration camps, 370
—, parenteral, by intravenous fat emulsions, 568
—, —, complete, in dogs, 230
— in Newfoundland, survey of, 1
—, infection in children and, 148
— without animal protein in emaciation, 7

Obesity, causes and treatment, 487
—, extracellular fluid volume in, 260
—, sudden, and psychological trauma, 532
Obstetric practice, survey of early, 560*
Oedema, acute vernal, 296
—, angioneurotic, acute intussusception in, 608
—, chronic and unexplained, 256
—, electrocardiograms and, 263
—, electrolyte partition in, 33
—, facial, in codeine poisoning, 134
— fluid, removal by Southey–Leech tubes, 611
— in penicillin-sodium–*p*-aminohippurate therapy, 580
—, pulmonary, mechanism of formation, 499
Oesophagus, 634–5
—, atresia of, with tracheo-oesophageal fistula, 229
— carcinoma, cytological diagnosis, 38
— —, rotation technique for radiotherapy, 589
—, " curling ", amyl nitrite and amphetamine in, 634
—, developmental anomalies, 342
— lesions in sclerodactyly, 69
— — — scleroderma, 634
—, lower end, anatomy and function, 342
—, motility, 284
—, peptic ulcer of, 283
—, short, review of 31 cases, 634
Oestrogen(s), haematopoiesis and, 277
— inunction, pilosebaceous system and adrenals of rabbit and, 76
— precursor, storage mechanism of, 77
Oestrus in sexually mature mice, penicillin and, 351
Oil particles in lung, bronchiogenic carcinoma and, 632
Old age, acid phosphatase of brain in, 309
— — and chronic sickness, 1, 113
— —, cardiology of, 375
— —, dermatoses in, 509
— —, gastric ulcers in, 636
— —, mental disturbances in, 207
— —, thyrotoxicosis in, 641
Onchocerciasis, " hetrazan " in, 333
Onychomycosis, differential diagnosis and treatment, 187
— due to *Mycotorula albicans*, 79
Ophthalmology in Seville in eighteenth century, 560*
Ophthalmoplegia in diabetes mellitus, 53
Orchitis, mumps, diethylstilboestrol in, 318
Oriental sore in Argentina, 441
Orthopaedic surgery in sixteenth and seventeenth centuries, 112*, 448*
" Orthoxine " in bronchial asthma, 369, 485
— — — —, spirometric evaluation, 260
— — bronchospasm, 279
Osler, William, 1849–1949, 336*
— on miner's phthisis, 224*
Osseous system disorders, 85–7, 306, 405–7, 518–23, 648–9
Osteoarthritis, intra-articular injection of acid in, 649
Osteogeny, Frederick Oldfield Ward, pioneer of, 560*
Osteoporosis in concentration camp, 592
Ovarian cysts, typhoid infection of, 321
— function, methyl- and propylthiouracil and, 640
— insufficiency, association with coarctation of aorta, 184
Oxophenarsine hydrochloride, lupus erythematosus discoides treated with, 80
— —, penicillin and, in experimental syphilis, 645
Oxygen blood saturation in polycythaemia vera, 277
— consumption, measurement in man, 157
— deficiency, acute, cocaine and ephedrine in, 574
— —, anaemic, sensitivity of respiratory centre to, 457
— —, effect on transient ventricular fibrillation and standstill, 57
— —, human kidney and, 196
—, haemotoxic role in high-altitude flight, 569
—, hypertension treated with, 60
—, neurological effects in chronic cor pulmonale, 491
— therapy, evaluation, 465
Oxyuris, retrograde infection with, 446
— *vermicularis*, pulmonary fibrosis and, 630
Ozone water, *Entamoeba histolytica* and, 439

Padua Medical School, figures and teachers in, 224*
Paediatrics, 46–7, 148–50, 255–8, 365–7, 479–84, 606–10
Pain, asymbolia for, 91
—, congenital universal indifference to, 92
—, ischaemic muscle, inhibition of water diuresis by, 231
Pain thresholds in man, antipyretic drugs and, 570
Palsy, Brödel's ulnar, historical notes, 560*
—, cerebral, " myanesin " in, 483
—, facial, of central origin, 408
" Paludrine ", *see* Proguanil
Pamaquine poisoning in man, 22
Pancreas, 71–3
— atrophy in infants with fatty liver, 150
— extract as growth stimulant for *Corynebacterium diphtheriae*, 254
—, fibrocystic disease, pulmonary lesions in, 390
—, — —, — —, aureomycin in, 631
—, — —, therapy and prognosis, 150
— function, mecholyl–secretin and morphine–secretin tests of, 283
— —, secretin test of, 72
—, islets of Langerhans, dextrose administration and, 359
—, lipomatous pseudohypertrophy with absence of exocrine tissue, 143
—, lipotropic factor, cholesterol deposition in liver and, 249
—, — —, toxic fatty infiltration of liver and, 248
— tumours, primary, in rats fed *p*-dimethylaminoazobenzene, 248
Pancreatitis, chronic, clinical and pathological findings, 633
—, —, peripheral pain in, 633
—, — recurrent, diagnosis, 73
—, — relapsing, total faecal solids, fat, and nitrogen in, 71
—, secretin test in, 72
Panhaematopenia, primary splenic, 277
Panmyelosis, 170
" Panparnit ", *see* " Parpanit "
Papaverine in angina pectoris, 267
Papaverine–heparin in peripheral arterial embolism, 623
Paracelsus as chemist, 560*
—, cosmology of, Basle pamphlet on, 336*
—, surgical lectures in Basle, 1527–8, 224*
Paraesthesia, post-ischaemic, 204
Paraldehyde in status epilepticus, 313
Paralysis, familial periodic, 413
—, gynaecomastia in, 77
—, spastic, " intocostrin " in, 650
—, unilateral, of sternomastoid and upper fibres of trapezius, 307
Paraplegia, testicular examination in, 599
" Parathion ", insecticidal and toxic properties, 586
Parathyrotoxicosis, syndrome of, 505
Paratyphoid, chloramphenicol in, 321
— in infants, chloramphenicol in, 544
— B, chloramphenicol in, 660, 661
Parergon, 560*
Parkinsonism, " artane " in, 414
—, artificial jaundice in, 309
—, " diparcol " in, 91
—, electrical activity of neostriatum and paleostriatum, 199
—, " parpanit " in, 530
—, pyramidotomy in, 202
—, raised metabolic rate in, effect of " parpanit " and " diparcol " on, 313
—, thiodiphenylamine derivative in, 413
—, trihexyphenidyl in, 530
Parotitis, *see* Mumps
" Parpanit ", central action of, 14
—, effect on decerebrate rigidity, spinal reflexes, and skeletal muscle, 124
—, — — raised metabolic rate in Parkinsonism, 313
— in diseases of basal ganglia, 651
—, pharmacological and toxicological studies, 15
Pathology, 33–40, 142–3, 247–52, 359–61, 474–6, 595–602
—, clinical, 38–40, 249–50, 600–2
—, experimental, 34–6, 247–9, 595–8
Pavlov, I. P., in development of internal medicine, 448*
" Pelentan ", clinical trials, 354
— in disseminated sclerosis, 200
Pellagra, insulin hypersensitivity in, 488
Pemphigus neonatorum, epidemiology in maternity hospitals, 565
— vulgaris, streptomycin in, 298
Penicillin, 20–1, 127–30, 235, 351–2, 580–1
— absorption, aerosol and intratracheal, 499
— action, borrelidin and, 18
— —, effects on activity of alkaline phosphatase, 42
— — in anaerobic infections, 253
— — — oestrus of mice, 351
—, clotting activity of blood and, 130
— diffusion through membranes, 130
— excretion in milk, 20
— G activity, 128
— — in early syphilis, 302
— — — experimental syphilis, 645
—, heated, vaccinia virus and, 603
—, impure, non-specificity, 21
— in abortive treatment of syphilis, 301
— — chronic suppurative disease of lung, 279
— — congenital syphilis, 82, 301
— — diphtheria carriers, 322, 544
— — — of newborn, 545
— — early syphilis, 302, 515, 645
— — — —, serological findings in, 192
— — gonococcal arthritis, 85, 194
— — gonorrhoea, 646
— — — prophylaxis, 193, 300
— — influenzal meningitis, 99, 324
— — late neurosyphilis, 192
— — lung abscess, 389
— — neurosyphilis, 400, 516
— — oil and wax in syphilis, 515
— — — with aluminium monostearate, 516
— — pneumococcal meningitis, 423
— — pulmonary suppuration, 173
— — rheumatic fever, 657
— — — — in children, 446
— — — — prophylaxis, 446
— — scarlet fever, 422
— — *Staphylococcus aureus* infections, 129
— — streptococcal endocarditis, 618
— — subacute bacterial endocarditis, 129, 159, 376, 491
— — tabes dorsalis, 203
— — tissue exudates after injection, 580
—, Jarisch–Herxheimer reaction and, 191

Penicillin level in blood, effect of benzoic acid and caronamide on, 129
— — — cerebrospinal fluid, 129, 351
— –malaria in tabes dorsalis, 203
— — — neurosyphilis, 645
—, " mapharsen " and bismuth salicylate with, in experimental syphilis, 645
—, mass prophylaxis against intercurrent infections, 235
—, peripheral nerves and, 129
— plasma concentration, effect of caronamide on, 20
— preparations and theory of accumulation, 130
— —, oral, comparison, 580
— -procaine and -sodium, comparison, 351
— — in children, 20
— — — syphilis, 192
— — preparations, clinical trials, 127
— — with aluminium monostearate in adults, 580
— — — — — — children, 127
— — G, blood and urine levels, 351
— resistance of *Staph. aureus*, 41
— -resistant organisms, sensitization of, 128
— — staphylococcal bacteriaemia, aureomycin in, 132
— — — infection, 253
— — staphylococci, bacteriophage types in, 253
— — —, origin, 144
— — *Staphylococcus pyogenes* in hospital, 362
—, root growth of seedlings and, 20
—, Shwartzman phenomenon with, 235
— sensitivity, *Actinomyces bovis* and, 42
— —, penicillinase - producing *Staph. pyogenes* and, 42
— -sodium *p* - aminohippurate therapy, oedema and potassium loss in, 580
—, subcurative doses, 515
—, sulphanilamide and, in *Erysipelothrix rhusiopathiae* infection of mice, 188
— –sulphathiazole, typhoid carriers and, 544
—, vehicles and adjuvants for, 17
Penicillinase activity, sulphonamides and, 352
Pentamethonium iodide, hypertension and, 271
— —, peripheral circulation and, 272
" Pentaquin " in malaria, 219
Pentothal, *see* Thiopentone
Pepsin secretion, histamine and, 177
Periarteritis nodosa, asthma and, 50
— —, sternal bone marrow examination in, 61
Periarthritis, humero-scapular, with bursal calcification, 470
Pericarditis, acute serofibrinous, 616
—, exudative, 155
— in bacterial endocarditis, 156
— — Finland, 155, 374
Pericardium, 155–6
—, adherent, and constrictio cordis, 155
Peridurography, 31
Periodic disease, review, 485
Peritoneum lavage in uraemia, comparison with artificial kidney, 83
Personality, narcoanalysis and " methedrine " shock in exploration of, 317
Perspiration, *see* Sweat
Pertussis, altitude flying and decompression treatment, 100, 213
Pertussis, aureomycin in, 19
—, chloramphenicol in, 661
—, hyperimmune human serum in, 423
— immunization, early, 545
—, " polymyxin B " in, 132
—, pulmonary complications, streptomycin in, 213
—, serotherapy, 322
—, streptomycin in, 236
— vaccine prophylaxis, encephalopathy after, 527
—, visammin in, 661
Petit mal, " tridione " in, 312, 530
Petroleum ingestion, pneumonia in children after, 581
Pharmacology, 10–25, 121–36, 232–41, 346–54, 458–66, 570–86
Pharyngo-laryngeal area, tuberculosis of, streptomycin in, 430
Pharynx, bacterial flora, comparison with nasopharynx, 603
" Phenergan " and " anthisan " as antihistaminics, 49
— in chronic gastritis, 177
Phenindamine, eczematous sensitization to topical application, 368
— in common cold, 539
— — disseminated and circumscribed lupus erythematosus, 297
— — gastro-intestinal allergy, 368
Phenosulfazole in poliomyelitis, 419, 420
Phenylarsenoxide, mode of action, 82
2-Phenylbenzylaminomethyl imidazoline, *see* " Antistin "
Phenylcyclopentane carboxylic acid, diethylaminoethyl ester of, *see* " Parpanit "
Phenylsemicarbazide, antipyretic action, 570
Phlebitis and thrombo-angiitis obliterans, 623
—, curare in, 490
Phlebotomus, *see* Sandfly
Phosphatase, acid, in the senile brain, 309
—, alkaline, penicillin and, 42
Phosphorus, radioactive, in chronic lymphatic leukaemia, 169
—, —, in gastric acidity suppression, 177
—, —, — polycythaemia vera, 386, 387
—, —, intraneural injection, fate of, 9
—, —, *Myco. tuberculosis* labelled with, 427
—, —, uptake by gastric carcinoma, 635
Phrenicolasis in pulmonary tuberculosis, 434
Phrenicotomy and pneumothorax in pulmonary tuberculosis, 553
Phrynoderma, association with hypothyroidism and vitamin-A deficiency, 78
Phthalylsulphacetimide in cholera, 213
" Physeptone " and isomers, clinical evaluation, 571
— — morphine, comparison, 10
Physical fitness, haemoglobin concentration and, 567
— —, resting pulse rate, blood pressure, and, 567
Physiology, 7–9, 119–20, 230–1, 343–5, 454–7, 567–9
Pick's disease, pathological study, 309
Pilocarpine, fatal poisoning after normal dose, 464
Pinel's conception of psychopathic state, 447
3-(N-Piperidyl)-1-*cyclo*hexyl-1-propanol hydrochloride, *see* " Artane "
Pitressin and deoxycortone acetate, antagonistic actions, 290
—, effect on sodium, potassium, and water excretion by dog, 290
— in cholecystography, 158
Pituitary, 185, 641–3
— adenoma, *x*-ray therapy, 244
— –adrenal function, rheumatic disease and, 518
—, anterior, gonadotrophin of, 291
— basophilism and eosinophilism, radiotherapy in, 356
— —, glucose tolerance tests in, 74
— —, radon implantation for, 335
— —, review, 185
— — syndrome, 643
—, gonadotrophic function, 185
— growth hormone, blood sugar level and, 119
— implantation in hypophysial disturbances, 291
— — — rheumatoid arthritis, 649
Pituitrin and polyvinyl–pyrrolidine in diabetes insipidus, 185
Pityriasis rubra pilaris, liver function in, 80
Placenta abruptio in vitamin-E deficiency, 119
— blood, transfusion of, 24
— permeability to lymphogranuloma venereum virus, 402
— praevia, radiological diagnosis, 358, 593
Plague of the Philistines, 559*
—, yellow, history, 447
Planigraphy, *see* Tomography
Plasmodia, survival in preserved blood, 25
Plasmodium berghei, response of cotton-rat to, 669
— *falciparum*, acquired resistance to proguanil, 443
— —, pre-erythrocytic stage, 558
— *gallinaceum*, action of quinine and of immunity on, 331
— — in chick, aureomycin and, 671
— —, mosquitoes infected with, antimalarial drugs and, 108
— *vivax*, Chesson strain, effect of antimalarial drugs on, 443
— —, — —, prophylactic action of aureomycin, 671
Pleural effusions, mechanism of, 501
— " shock ", 501
— thickening, localized, respiratory changes in differential diagnosis, 246
Pleurisy, mediastinal, 388
Pleuropneumonia-like organisms in rheumatic diseases, aureomycin and, 405
Pneumatosis, cystic, of sigmoid, 179
Pneumococcus types, frequency in Denmark, 1939–47, 41
Pneumoconiosis, coal - miners', 228
— in graphite workers, 453
—, sulphur dioxide fumes producing, 566
—, talc, 228
Pneumonia and empyema due to *Nocardia asteroides*, 417
—, atypical, chloramphenicol in, 282
—, —, Q fever and, 541
— due to meningopneumotrophic virus, 95
—, Friedländer, acute, 282, 357
— in children, ingestion of petroleum producing, 581
Pneumonia in infants and children, aureomycin in, 237
— — newborn due to inhalation of gastric contents, 482
—, lobar, sterile serous effusions after sulphonamide treatment, 175
—, post-pertussis, streptomycin in, 213
—, primary atypical, aureomycin in, 174, 237, 238, 631
—, — —, — and chloramphenicol in, 657
—, — —, infectiousness and incubation period, 565
—, suppurative, non - specific, 281
Pneumonitis, acute, in a beryllium worker, 6
—, chronic, 500
—, —, of cholesterol type, 174
Pneumonolysis, extrapleural, with " lucite " plombage, in pulmonary tuberculosis, 553
Pneumoperitoneum, artificial, complicated by spontaneous pneumothorax, 280
Pneumotherapy, cerebral, 535
Pneumothorax and phrenicotomy in pulmonary tuberculosis, 553
— — streptomycin in pulmonary tuberculosis, 216
—, artificial, induction in the home, 427
—, —, in pulmonary tuberculosis, 103
—, —, remote results, 102
—, effect on bronchus, 669
—, electrocardiographic patterns in, 151
—, extrapleural, post-operative complications, 668
—, periodical spontaneous, coinciding with menstrual cycle, 501
—, spontaneous, 105 cases, 388
—, —, complicating artificial pneumoperitoneum, 280
Podophyllum resin, warts treated with, 81
Polio-encephalitis due to poliomyelitis virus, 319
Poliomyelitis, 419–20
—, acute anterior, spasm and paralysis in, 318
—, —, severity and distribution of lesions of medulla oblongata in, 538
—, —, sympathetic nervous system involvement in, 69
—, anterior, exercise and curare in, 210
—, —, intraspinal pyridoxine and aneurin in, 538
—, bulbar, treatment as problem in respiratory obstruction, 420
—, epidemic apoplexy and, 658
— epidemiology in Dorset, 5
— — — New Zealand, 5
— in the Arctic, 450, 451
— incidence, 565
—, micturition disorders in, 319
—, non-paralytic, disease resembling, 539
—, phenosulfazole in, 419, 420
—, prodromal illness in Berlin epidemic, 1947, 419
— production, acceleration of, 319*
—, seventeenth-century case of, 335
Pollen, allergic specificity of, 486
Polyarthritis, experimental, aureomycin in, 198
—, —, thiouracil and thyroidectomy in, 87
Polycythaemia vera, blood coagulation in, 360
— —, — oxygen saturation in, 277
— —, circulatory and respiratory function in, 385

Polycythaemia vera, radioactive phosphorus in, 386, 387
— —, serum proteins in, electrophoretic analysis, 62
Polygamy and population in eighteenth century, 224*
Polyganglioneuritis, 204
" Polymyxin B " in pertussis, 132
— —, laboratory and clinical observations, 132
—, clinical use, 461
— in experimental brucellosis and tularaemia, 662
Polyneuritis, calciferol treatment and, 644
Polyp, gastric, differential diagnosis, 591
Polysaccharide, serum levels of, 249
Polyvinyl-pyrrolidone and pituitrin, diabetes insipidus treated with, 185
Population and polygamy in eighteenth century, 224*
Porphyria, acute, and associated electrolytic changes, 51
—, — idiopathic, presenting as progressive paresis of Landry type, 612
—, —, sodium and chloride depletion in, adrenal cortex and, 50
Posture, cerebral circulation in man and, 653
— in pulmonary tuberculosis, 435
—, venous and right auricular pressure and, 343
Potassium blood concentration in therapy of diabetic acidosis, 53
— deficiency, kidney in production of, 403
— excretion, pitressin and desoxycortone acetate and, 290
— in dialysing fluid in artificial-kidney treatment, 83
— — prolonged insulin coma, 317
— iodide in cholesterol-induced atherosclerosis, 163
— loss in penicillin–sodium *p*-aminohippurate therapy, 580
— metabolism in diabetic acidosis, 373
—, relation to neurological manifestations of hypocalcaemic tetany, 51
—, serum, in diabetic acidosis, 262
Pott, Percivall, 336*
Pottery industry, lead poisoning in, 239
— —, silicosis in, 341
Potts's operation for congenital pulmonary stenosis, 58
Pregnancy, disseminated sclerosis and, 308
—, electric shock therapy of psychosis in, 655
—, heart disease in, 617
—, idiopathic epilepsy and, 414
— in Addison's disease, 183
—, normal, duration of Q–T interval in, 155
— toxaemias, cardiovascular system in, 616
" Pregnenolone " in rheumatoid arthritis, 519
Prickly heat, water and salt intake and, 295
" Priscol ", peripheral circulation and, 13, 572
— treatment and sympathectomy compared, 268
Procaine, contact dermatitis due to, 296
—, intravenous, effect on heart, 232
—, —, in arthritis, 519
— penicillin, *see* Penicillin-procaine
Procaine, shock prevention by, during protein hydrolysate infusion and blood transfusion, 241
Progesterone in rheumatoid arthritis, 648
Proguanil in malaria in Indo-China, 108
— -resistant *Plasmodium falciparum* malaria, 443, 669
— treatment and prophylaxis of malaria, 670
Promin in tuberculosis, 328
— — tuberculous meningitis, 432
" Promizole " and streptomycin in miliary tuberculosis and tuberculous meningitis, 217
— in pulmonary tuberculosis, 668
N-*iso*Propylarterenol, *see* " Isuprel "
Propylthiouracil in thyrotoxicosis, 182, 640
Prostigmin, *see* Neostigmine
Protamine, blood coagulation and, 459
—, heparin action neutralized by, 459
Protein, Bence-Jones, of multiple myelomatosis, 171
— deficiency in essential hypertension, 622
— —, prolonged, structure of nucleus in, 476
— depletion, effect of choline on liver during, 289
— hydrolysate, buffering capacity, 71
— — infusion, shock prevention by procaine, 241
—, intact and pre-digested, comparative buffering capacity, 71
— metabolism, prolonged thiopentone and, 121
— requirements in marasmus, 606
—, resistance to tuberculosis and, 214
—, serum, in blood dyscrasias, 62
—, —, — liver cirrhosis, 289
—, —, structure and liver function in gout, 52
Prothrombin consumption in blood coagulation, haemophilia and, 382
— — test, clinical and theoretical implications, 601
— determination by stabilized thrombin method in control of dicoumarol therapy, 476
— in human blood, 361
— — — — in parenchymatous hepatitis and obstructive jaundice, 252
— time, Link–Shapiro modification of Quick's test for, 601
— —, measurement and factors affecting, 584
— —, streptomycin effect on, 22
Protozoal infections, 105–6, 219–20, 330–2, 439–41, 556–7
Pruritus ani, radiotherapy, 29
—, riboflavin in, 80
—, tetraethylammonium chloride in, 189
Psittacosis in chick embryo, action of aureomycin and chloramphenicol on, 461
Psoriasis, arthritis and, adrenocorticotrophin in, 642
—, calciferol in, 79, 81
— in the Tropics and in starvation camps, 297
—, liver function in, 295
—, undecylenic acid in, 189
Psychiatry, 94, 207–8, 315–17, 415–16, 532–6, 654–5
Psycho-galvanic reflex, nervous pathway of, 120
Psychosis, adrenal cortical function in, 654
—, endogenous, acute infections and, 94
Psychosis, group and individual therapy, 655
—, hyperthymic, delimitation from chronic mania and hypomania, 316
— in pregnancy, electric shock therapy, 655
—, physical disorders in, 94
—, unrecognized late post-encephalitic states, 415
Psychosomatic medicine, 532–4
Pteroylglutamic acid, *see* Folic acid
Public health, 1–6, 113–17, 225–8, 337–41, 449–53, 561–6
Pulse rate, physical fitness and, 567
Pupil, tonic, study of, 307
Purpura annularis telangiectodes, 398
— associated with infections, 498
— haemorrhagica, sarcoidosis and, 274
—, idiopathic thrombocytopenic, 498
—, " sedormid ", blood-clot retraction by, 497
—, —, cause of thrombocytopenia in, 498
—, thrombocytopenic, after rubella, 498
—, —, coagulation defect in, 168, 258
—, —, during TB I/698 administration, 550
—, —, " sedormid " hypersensitivity and, 66
Pyelography by rapid injection of " neo-iopax ", 246
Pylorospasm, recurrence after operation, 482
Pylorus, hypertrophic stenosis, genetic study, 118
— in evacuation of stomach, 390
— stenosis, infantile hypertrophic, 32
Pyocyaneus sepsis, polymyxin in, 462*
Pyogenic infection, bacitracin in, 188
Pyothorax, chronic tuberculous, 429
Pyranisamine maleate, *see* " Anthisan "
Pyrexia in infants, sustained summer heat and, 46
" Pyribenzamine ", dermatitis after, 644
—, skin reactions to, 49

Q fever, atypical pneumonia and, 541
— —, aureomycin in, 542
— — epidemiology, sheep and goats in, 115
— — in Italy, with pulmonary and phlebitic involvement 541
— — — man and animals, 542
— — — Spain, 321, 541
— —, radiological manifestations, 472
Quinine in Chesson strain *Plasmodium vivax* malaria, 443
— — *gallinaceum* malaria, spleen and, 331
— methochloride, pharmacological properties, 125

Rabies in Danubian States, 225
Radiation, ionizing, chemical measurement, 355
—, measurement of a dose at depth in tissue, 137
— sickness, dramamine in, 242
Radioactive elements created by nuclear fission, metabolism, 28
Radiodermatitis of lip after exposure to arc welding, 117
Radiodiagnosis, 31–2, 138–41, 245–6, 356–8, 471–3, 590–4
Radiography, mass miniature follow-up, 426
—, protection of personnel, 137
Radiotherapy, 29–31, 242–5, 355–6, 470–1, 588–90. *See also X*-ray irradiation
—, supervoltage, 243
Radium deposits in bone, 137
— poisoning, occupational, 468
— therapy at operation for cerebral glioma, 471
— — of bladder carcinoma, new technique, 244
— — — cervical carcinoma, 245
— — — rectal carcinoma, 30
Radon implantation for acromegaly and Cushing's syndrome, 355
Raynaud's disease, arteriography in, 61
— phenomenon in workers with vibratory tools, 227
Rectum, carcinoma, high-voltage *x*-ray therapy, 30
—, —, radium treatment, 30
—, irradiation injuries, late reactions, 470
Reflex, psycho-galvanic, nervous pathway of, 120
—, skin–lung, in pulmonary tuberculosis, 554
Renal, *see* Kidney
Renin in blood of hypertensive patients, 381
Renninogen in urine in pernicious anaemia, diagnostic value, 275
Resins, synthetic, in gastric ulcer, 392
Respiration, decamethonium iodide effect, 11
— in pulmonary anoxaemia, 174
—, mechanical, indications for, 48
Respiratory centre, sensitivity to anaemic hypoxia, 457
— disease, air pollution in towns and, 562
— **disorders,** 67–8, 172–5, 279–82, 388–9, 499–501, 629–32
— infection, handkerchiefs in transfer of, 67
— **system,** 457
— tract, bacterial flora, single throat culture as index of 562
— —, congenital obstructions, 255
Rest, cardiovascular function and work performance and, 611
Reticulo-endothelial system, 65, 171, 278, 387
Reticuloses, nitrogen mustard in, 171, 625
Retina, arterial occlusion, in migraine, 531
—, vascular occlusion, nature of infarcts following, 33
Rh factor, *see* Blood groups
Rheumatic fever, 446. *See also* Rheumatism, acute
— — in children, penicillin in, 446
— —, recurrent, penicillin prophylaxis, 446
Rheumatism, acute, 222–3
—, —, cardiac lesions in, experimental induction, 223
—, —, compound E in, 110
—, —, following acute tonsillitis, 334
—, —, heparin tolerance, 333
—, —, in war and post-war periods, 223
—, —, neuropathologica changes, 311
—, —, " phase " reaction and antibody detection in, 333
—, —, Q–T interval in, 537
—, —, recurrent penicillin prophylaxis, 657
—, —, salicylate therapy, 222
—, —, segmental colitis and 344

Rheumatism, acute, sulphanilamide prophylaxis, 334
—, *p*-aminobenzoic acid in, 87
—, calcium succinate and acetylsalicylic acid in, 405
—, chronic, and anterior pituitary hormones, 406
—, —, serum antitryptase in, 87
—, muscle spasm in, curare treatment, 405
—, pituitary – adrenal function and, 518
—, plasma viscosity in, 252, 405
—, pleuropneumonia-like organisms associated with, 405
—, "psychogenic", 198
—, senile prostatic, 518
—, streptococcic spreading factor and, 110
— syndromes, fibro-fatty tissue in relation to, 198
—, synovial fluid examination and biopsy in, 405
—, "TB 1/698" in, 102
Rhythm in work in hot shops, 566
Riboflavin deficiency in diet, 612
—, infant requirement, 454
—, pruritus treated by, 80
Ribs, premature calcification of, 306
Rice diet in essential hypertension, 622
— — — — — and arteriosclerotic vascular disease, 494
Ricin, allergic conditions in industry due to, 117
Rickets in newborn infants, 488
Rickettsiae, body lice, typhus vaccine and, 98
— *burnetii*, recovery from *Hyalomma savignyi* in Spain, 656
Rickettsial disease, aureomycin in, 542
— **infections,** 97–8, 320–1, 420–2, 540–3
— —, experimental, chloramphenicol in, 420
Rickettsialpox, clinical and laboratory study, 656
Rift Valley fever, laboratory infections of, 211
Ringworm, *see* Tinea
Rocky Mountain spotted fever, aureomycin in, 97
— — — —, liver and kidney function in, 540
Roman legions, medical service with, 672*
Roseola infantum, 149
Rubella, experimental production in man, 95
—, maternal, deafness in children due to, 255
—, thrombocytopenic purpura complicating, 498
Russian doctors, materialistic outlook in eighteenth century, 112

St. Gallen Monastery Infirmarium, A.D. 820, 559*
Salicylates, oral, in rheumatic fever, 222
Salmine, toxicity in different species, 134
Salmonella enteritis, chloramphenicol in, 662
— strains, isolation of, 603
— *typhi* 42–A–58, induction of active immunity to, 364
Salmonellosis, chloramphenicol in, 131
Salt, *see* Sodium chloride
Sandfly eradication, DDT in, 337
Sandstone workers, silicosis in, 341
Sarcoidosis, 278
—, calciferol in, 79, 625
—, Kveim reaction in, 387
—, miliary, 340
Sarcoidosis, osseous lesions, 246
—, possible fungal origin, 65
—, purpura haemorrhagica and, 274
—, tuberculosis compared with, 387
Sarcoma, folic acid derivatives in, 577
— growth, aminopterin in, 248
—, inhibition by virus of Russian Far East encephalitis, 248
Scabies, allergy in, 510
Scarlet fever, acute serous meningitis and encephalitis complicating, 99
— —, diagnosis, 422
— —, penicillin in, 422
Schick reaction, skin factor in, 147
Schistosomiasis eradication, 4
—, "fouadin" in, 221
— in mice, antimonials in, 221
— — New Zealand, 445
— japonica, 445
—, vesical, stibophen in, 332
Schizophrenia, 534–6
—, auditory hallucinations and subvocal speech in, 94
—, brain weight and changes in, 534
—, chronic, non-diabetic glycosuria in, 316
—, "confused", catamnestic investigations on, 415
—, electric shock in diagnosis, 208
—, electrothalamography in, 88
—, insulin in, follow-up, 208
—, prefrontal leucotomy in, 534
Schwannoma, spinal, myelography in, 140
Sciatica, disco-radicular, 307
—, prolapsed intervertebral disk causing, 409
—, root neuritis and, 650
Sclerodactyly, oesophageal lesions in, 69
Scleroderma, oesophageal lesions in, 634
—, pulmonary fibrosis in, 399
—, spinal and nervous system lesions and, 190
Scleroma, cytological diagnosis, 143
Sclerosis, disseminated, adrenocorticotrophin in, 525
—, —, anticoagulant therapy, 200
—, —, artificial jaundice in treatment, 309
—, —, copper sulphate in, 90
—, —, ethylene dicoumarin and, 89
—, —, follow-up study, 411
—, —, histamine in, 308
—, —, in South Africa, 90
—, —, pathology, 90
—, —, pregnancy and, 308
—, —, prognosis, 651
—, —, "solustibosan" in, 90
Scoliosis, cervico-thoracic cord disorders and, 91
Scotoma, visual, with intracranial lesions, 411
Scurvy in a Sudanese village, 488
—, tyrosine metabolism in, 487
Seabather's eruption, 295
Seasickness, *see* Motion sickness
Sebaceous glands, sex hormones and, 76
Secretin test, clinical studies, 72
— — in idiopathic steatorrhoea, 283
— — — pancreatitis, 72
"Sedormid" purpura, cause of thrombocytopenia in, 498
— —, reduction of blood-clot retraction, 497
—, thrombocytopenic purpura due to, 66
Semen plasma, heterologous, effect on fertilizing capacity of rabbit spermatozoa, 454
Sensation, electrical nvestigation, 307
— in hand after blood-flow arrest, 569
Sepsis in children, 148
Septicaemia due to *Bacteroides funduliformis*, aureomycin in, 324
— — — intestinal organisms in infants, streptomycin in, 149
Sex activity, role of hormones in, 184
— development disorders after brain injury, 526
Shigella pathogenicity, 565
Shock, haemorrhagic, vasodepressor responses to morphine after, 10
— therapy, electric, body temperature in, 317
— —, —, cortin and ketosteroid excretion and, 536
— —, —, diagnostic aid in schizophrenia, 208
— —, —, electroencephalogram in, 525
— —, —, impairment of consciousness after, 536
— —, —, in psychosis of pregnancy, 655
— —, —, modifications in, 416
— —, —, nikethamide with, in states of excitement, 208
— —, —, peripheral circulation in, 317
— —, insulin, in women, 536
Shoulder paralysis, isolated unilateral, 307
"Shoulder – hand" syndrome, complication of coronary artery disease, 267
Shwartzman phenomenon with penicillin, 235
Sickle-cell disease, pathological and clinical significance, 165
Sigmoid, cystic pneumatosis of, 179
Silica dust deposition in lungs, 341
Silicosis, cardiovascular effects, clinical examination, 452
—, cor pulmonale in, 264
— disability, evaluation, 452
—, "egg-shell" calcification in, 172
— in coal-miners, electrocardiography, 389
— — pottery industry, 341
— — sandstone workers, 341
—, Knipping–Scoz test in, 117
—, pulmonary hilar shadow changes in, 357
— silico-tuberculosis and, mortality and survival rates in males, 451
Simmonds's disease, anaemia and arthritis in, 643
Sinus, cavernous, applied anatomy in relation to embryological development, 229
—, tuberculous, antibiotics in, 550, 664
Skin, irradiation injuries, tubercle-like structures in, 29
— lesions associated with hypothyroidism and vitamin-A deficiency, 78
— –lung reflex, application to pulmonary tuberculosis, 554
—, mucinous infiltration, hyaluronidase in, 190
— reactions to pyribenzamine and adrenaline, 49
— transplantation in mice, 20-methylcholanthrene and, 507
— tuberculosis, calciferol in, 79
Skull injuries in ancient Egypt, 111
— vault tumours, radiological diagnosis, 590
Sleeping sickness, *see* Trypanosomiasis
Smallpox vaccination, introduction into U.S., 112*
— — in persons with history of post-vaccinal encephalitis, 563
— —, peripheral nerve and root disturbance after, 529
— —, *see also* Vaccinia
— vaccine, herpes multiplex and, 80
Sodium-*m*-(allylcuprothiocarbamido)-benzoate in rheumatoid arthritis, 85
— *p*-aminosalicylic acid, resistance of *Myco. tuberculosis* to, 126
— bismuth triglycollamate in dermatology, 295
— carboxymethylcellulose in duodenal ulcer, 391
— — as laxative, 394
— chloride aerosols, effect on dust in lungs, 341
— — and water distribution in heavy sweating, 7
— — — — intake in prickly heat, 295
— —, hypertonic solution, renal responses, 231
— — in experimental hypertension, 620
— —, influence on deoxycortone acetate, 183
— —, lithium chloride as substitute in diet, 581
— —, low extracellular, renal failure with, 305
— — restriction in hypertension, 494
— — tolerance test in adrenal cortex hyperfunction, 505
— excretion, adrenal cortex activity and, 343
— —, pitressin and deoxycortone acetate and, 290
— ions, quaternary, in nerve physiology, 13
— nicotinate, hyperbilirubinaemic effect, 504
—, radioactive, in measurement of regional circulation, 267
— restriction in ambulatory hypertensive subjects, 380
— — — hepatic cirrhosis with ascites, 504
— and sodium salts, variations in intake, 344
— succinate in barbiturate poisoning, 581
— tetraiodophenolphthaleinate, *see* Iodophthalein
— thiocyanate, cardiac output and, 156
"Solustibosan" in disseminated sclerosis, 90
"Sontoquine", *see* Chloroquine
Soy-bean fat, utilization of, 343
Sparteine, sulphate as diuretic 16
Speech, subvocal, in schizophrenia, 94
Sperm cells, heterologous, fertilizing capacity of rabbit, 454
Spherocytosis, hereditary, *see* Jaundice, familial haemolytic
Spinal cord, 528–9
— —, cervico-thoracic, scoliosis as manifestation of disease of, 91
— — degeneration in pernicious anaemia, 412
— — disease, electroencephalography in, 410
— — lesions in achondroplasia, 203
— —, postero-lateral column and hepato-lenticular degeneration, 310
— —, subacute combined degeneration, vitamin B_{12} and liver extract in, 525
Spine, epidural space, injection of radiopaque substance into, 31

Spine, intervertebral disks and vertebral ligaments, herniated, radiological diagnosis, 592
— lesions, scleroderma and, 190
—, lumbar-sacral, congenital abnormalities, 32
—, nerve root area, anatomy, etc., 528
—, *see also* Vertebrae
Spleen, panhaematopenia of, 277
—, quinine treatment of *gallinaceum* malaria and, 331
—, tuberculous, radiographic picture, 246
Splenectomy, chronic neutropenia and, 170
—, cyclical agranulocytosis and, 273
Spondylitis, ankylosing, cardiac complications in, 156
—, —, pulmonary disease manifestations of, 198
—, —, statistical studies, 86
—, rheumatoid, familial incidence, 86
—, —, *d*-tubocurarine in oil–wax in, 86
—, tuberculous, tomography in, 592
Sponge, radiopaque, radiological recognition after abdominal operations, 31
Sprue, aetiology, dietary fat in, 633
—, diagnosis and pathogenesis, 393
— in India, 178
—, non-tropical, *see* Steatorrhoea
—, proteolytic activity *in vitro* of gastric juice in, 178
— syndrome, fat metabolism and, 370
—, vitamin-A absorption in, 178
—, — B_{12} in, 276, 486
Sputum examination in pulmonary adenomatosis, 500
— in pulmonary tuberculosis, *Candida* in, 363
— volume, effect of mood and emotional stress on, 316
Staphylococci, penicillin-resistant, bacteriophage types in, 253
Staphylococcus aureus in anterior nares of children, 362
— — infections, penicillin in, 129
— —, penicillin-resistant, 41, 144, 253
— infections, aureomycin in, 238
— *pyogenes*, infantile diarrhoea and vomiting and, 481
— —, penicillin- and streptomycin-resistant, 362
— —, — sensitive variant colonies in penicillinase-producing strains of, 42
Staphylotoxin immunity in diabetes, anatoxin and, 44
Starvation, rehabilitation without animal protein in, 7
Steatorrhoea, fat absorption in, 610
—, — metabolism and, 370
—, glossitis and, after ileocolostomy, 288
—, idiopathic, duodenal secretion in, 283
Sterility, male, 3,182 cases, 647
Sterilization of men, late effects, 8
Sternum puncture and intrasternal infusions, dangers of, 475
Steroid compounds, rheumatoid arthritis and, 520
"Sterosan", topical, in dermatoses, 398
Stibophen in *Schistosoma haematobium* infection, 221
— in vesical schistosomiasis, intensive treatment, 332
Stilbamidine, retention in body, 105
Stilbamidine, nervous system toxicity to, 105
Stillbirths in Czechoslovakia, 480
Still's disease, hormone effect, 522
Stomach, 69–71, 176–8, 284–7, 390–3, 502–4, 635–7
— acidity, *see* Gastric acidity
— activity, suppression with radioactive phosphorus, 177
— carcinoma, differential diagnosis, 31
— —, electrogastrography in, 391
— —, location and extent, gastroscopy in, 71
— —, radioactive phosphorus uptake by, 635
—, cardia, carcinoma, cytological diagnosis, 38
— —, —, radiodiagnosis, ineffectiveness of, 141
—, double contrast radiographs of, 141
— and duodenum of hog, haematopoietic factors in, 165
— evacuation, pylorus in, 390
— granuloma, submucosal, with eosinophilic infiltration, 37
— involvement in malignant lymphoma, 71
— mucosa, appearance in vagotomy for peptic ulcer, 287
— —, prolapsed, radiodiagnosis, 140
— mucus secretion, 40
—, polyposis, radiological diagnosis, 591
—, radiography, morphine and ipecacuanha in, 141
— secretion, *see* Gastric secretion
— shape, significance for ulcer formation, 473
—, upper, carcinoma, diagnostic difficulties in, 635
—, volvulus, diagnosis, 637
—, —, in infants, radiology of, 591
Strange, John, and Switzerland, 448*
Streptococcus, haemolytic, spreading factor in rheumatic patients, 110
— *viridans*, serological classification, 254
Streptomyces fradiae, antibiotic neomycin from, 237
Streptomycin, 21–2, 235–6
— absorption and breakdown in colon, 348
— abuse in pulmonary tuberculosis in childhood, 328
— activity, differential effects of various electrolytes on, 43
—, altitudinal hemianopia due to, 130
—, antibacterial activity, inhibition by cerebrospinal fluid, 21
—, *Bact. coli* resistant to or dependent on, 604
—, — *tularense*, effect on, 424
—, bacterial flora of throat and, 22
—, blood clotting and prothrombin times in man and, 22
—, brucella and, 131, 323
—, encephalitis, fatal toxic, due to, 348
—, equilibrium disturbances due to, 131
— in anaerobic infections, 253
— — Crohn's disease, 393
— — cutaneous tuberculosis, 511
— — enterocolitis, 551
— — *Haem. influenzae* meningitis, 99, 484
— — miliary tuberculosis, 430, 665
— — non-specific infantile diarrhoea and vomiting, 256
— — pemphigus vulgaris, 298
— — pertussis, 236
Streptomycin in pharyngolaryngeal tuberculosis, 430
— — post-pertussis pneumonia, 213
— — pulmonary tuberculosis, 430, 433, 666
— — *Shigella* enteritis, 423
— — subacute bacterial endocarditis, 235
— — transplacental congenital tuberculous meningitis, 431
— — tuberculosis, 216, 552
— — — in children, 328, 665
— — —, mechanism of action, 215
— — —, pharmacological and therapeutic action, 328
— — tuberculous adenitis, 430
— — bronchopneumonia in children, 104
— — meningitis, 104, 431, 666
— — —, cerebrospinal fluid changes during, 432
— — sinuses, 550
— — tularaemia, 424
— — urinary tuberculosis, 328
— — urogenital tuberculosis, 551
— level in cerebrospinal fluid in dogs with *Bact. coli* meningitis, 202
—, morphology of growth of *Myco. tuberculosis* and, 43
—, neurotoxic properties, 21
—, pneumothorax and, in pulmonary tuberculosis, 216
—, "promizole" and, in tuberculosis and meningitis, 217
—, repeated aspiration and, in tuberculous empyema, 551
— resistance of Gram-negative bacilli, 145
— — — *Myco. tuberculosis*, 552
— — — — —. *p*-aminosalicylic acid and, 103
— — — — —, influence of various factors in, 104
— — — — —, pulmonary cavitation and development of, 104, 433
— -resistant *Staphylococcus pyogenes*, incidence in hospital, 362
— sensitivity of *Actinomyces bovis*, changes in, 42
— — of bacteria, 21
— — — *Myco. tuberculosis*, 105*
—, septicaemia and meningitis in infants treated with, 149
—, toxic effects, 578
—, — —, ratio of dosage to body weight and, 236
—, — — on vestibular apparatus, 130
— -treated tuberculosis, tuberculin allergy and erythrocyte sedimentation rate in, 430
— — tuberculous meningitis, follow-up, 606
"Streptothricin VI", production, isolation, and antituberculosis properties, 19
Sturge–Weber syndrome, location of focus of epileptic discharge by electroencephalography, 650
Subtilin, tuberculostatic effect, 103
Succinic acid in bronchial asthma, 151
— — — —, spirographic study, 369
Sucrose–iron preparation in anaemia, 62
Sudan black B for staining of *Myco. tuberculosis*, 44*
Sugar, toxic effect on liver, prevention by choline, 595
Sulphadiazine and chloramphenicol in experimental typhoid, 349
— in congenital toxoplasmosis in mice, 220
Sulphamezathine and "benadryl" in infantile gastroenteritis, 149
Sulphanilamide and penicillin in *Erysipelothrix rhusiopathiae* infection of mice, 188
— prophylaxis in rheumatic fever, 334
Sulphathiazole in gonorrhoea, 82
— -penicillin, typhoid carriers treated with, 544
Sulphetrone in experimental tuberculosis, 328
— — pulmonary tuberculosis, 552
Sulphonamide(s) in common contagious diseases, 338
— — gonococcal arthritis, 85
— — malaria, suppressive action, 107
— level in blood in prophylaxis against *Plasmodium gallinaccum*, 108
— treatment, sterile serous effusions in, lobar pneumonia after, 175
—, vehicles and adjuvants for, 17
Sulphones in tuberculosis, pharmacological and therapeutic action, 328
Sulphur-dioxide fumes, pneumoconiosis from, 566
Sunlight, urticaria on exposure to, 187
Suprarenal cortex in genesis of rheumatic manifestations, 293
— **glands,** 76, 183–4, 293–4, 641–3
— —, effect on, of inunction with hormones, 76
— —, noradrenaline liberated from, 183
"Supronal" in subacute bacterial endocarditis, 159
Surgeons, barber, of Edinburgh, 560*
— of Preci and Norcia, 560*
Surgery, operative, first Russian textbook of, 224*
Sweat, biochemical changes in dermatomycoses, 79
— gland abscess, radiotherapy, 29
Sweating, antiperspirants, action of local, 298
—, heavy, salt and water distribution changes in, 7
Sycosis, subnasal, chronic relapsing, 188
Syme, James, 1799–1870, 224*
Sympathectomy, blood vessels of upper limb after, 163
—, haemodynamic effects in essential hypertension, 59
—, high dorsolumbar, in hypertension, 60
— in hypertension, 160, 621
—, "priscol", "etamon", and "dibenamine" effects compared with, 268
Syncope and seizures, 205
Synovial fluid in rheumatoid and rheumatic arthritis, 405, 649
Syphilis, 191–3, 301–3, 400–2, 513–16, 645–6. *See also Treponema*
—, abortive treatment, 301
—, arsenoxide preparations in, 514
—, aureomycin in, 303
—, blood serum in, treponemal immobilization of, 513
—, cardiovascular, penicillin in, 302
—, congenital, bone lesions in, penicillin and combined treatment, 82
—, —, penicillin in, 301
— contacts, prophylaxis, 82
—, cutaneous, late, aureomycin in, 19
—, Dattner–Thomas formula in cerebrospinal fluid in, 303

Syphilis, diagnosis by rapid slide-test, 314
—, early, aureomycin in, 400, 401
—, —, chloramphenicol in, 514, 646
—, —, penicillin treatment, 302, 645
—, —, — -treated, reinfection and relapse, 515
—, —, — —, serological findings in, 192
—, experimental, effects of crystalline penicillin G and impure penicillin on, 645
—, —, penicillin, " mapharsen ", and bismuth salicylate in, 645
—, gastric, pathology and gastroscopic diagnosis, 303
—, identity of bejel with, 301
—, jaundice in, 401
—, late, intradermal skin testing with " luotest " in, 401
—, neoarsphenamine and bismuth in, 514
—, penicillin in oil and wax in, 515
—, —— procaine in oil, 192
— reinfection, 191
Syringomyelia, familial lumbosacral, spinal developmental errors and, 90
—, *x*-ray treatment, statistics, 242

Tabes dorsalis, penicillin and penicillin–malaria in, 203
— — treatments, evaluation of, 192
Talc pneumoconiosis, 228
TB1, *see also* Thiosemicarbazone
— and Tb IV in cavernous pulmonary tuberculosis, 436
TB I/698, *see also* Thiosemicarbazone
— and TB IV in tuberculous meningitis, 549
— in lupus, side-effects, 189
— — tuberculosis and rheumatism, 102
— — —, pulmonary, 326, 666
— — tuberculous empyema, 549, 550
— treatment, haematological findings, 550
TB I/698 E, toxic effects, 550
Teeth, molar, erosion by acid beverages, 502
— opacity, fluorine poisoning and, 176
—, serological classification of *viridans* streptococci from, 254
Telangiectasis, primary diffuse, 512
Temperature extremes, hormonal alterations and, 182
—, low, heart injury in rabbits and, 611
—, —, vascular reactions in fingers, 568
— of tissue and arterial blood in resting human forearm, 456
Teropterin in pernicious anaemia, 383
— — sarcoma, 577
Testis changes in paraplegia, 599
Testosterone propionate absorption and excretion, mode of administration and, 77
Tetanus, hospital-infected cases, source of, 562
— toxin, gaseous products of growth and, 41
Tetany, hypocalcaemic, neurological manifestations, relation of potassium to, 51
Tetraethylammonium bromide, effect on gastric secretion and motility, 391
— —, — — kidneys, 123
— — in hypertension and peripheral vascular disease, 379
— —, sudden death from, 123
Tetraethylammonium chloride, effect on cardiovascular reactions to gravitational changes, 345
— —, — — peripheral blood flow, 268
— — in peripheral vascular disease, 271
— —, intravenous, effect on electrocardiogram, 154
— —, " itchy skin " inhibited by, 189
Tetraethyl pyrophosphate, effects in man, 122
— — in myasthenia gravis, 122
— —, sympatholytic effect, comparison with sympathectomy, 268
Tetraethylthiuramdisulphide, *see* " Antabus "
" Tetramycin ", antibiotic properties, 579
Thalamus, *état marbré* of, after birth injury, 203
" Thalamyd " in cholera, 213
" Thenfadil ", toxic properties, 463
Theophylline ethylene diamine and renal function in congestive heart failure, 617
" Thephorin ", *see* Phenindamine
Therapeutics, 24–5, 121–36, 232–41, 354, 465–6, 584–6
Thiamin, *see* Aneurin
Thioarsenates in amoebiasis, 440
Thiocyanate in hypertension, 620
— and thyrotropin, paradoxical effects on organic binding of iodine by thyroid, 293
—, toxic action, mechanism, 134
Thiocytosine in thyrotoxicosis, 293
Thiomerin, cardiopressive effects, 577*
— in congestive heart failure, 233
— toxicity, 233
Thiophanium derivatives, ganglionic blocking activity, 347
Thiosemicarbazone, *see also* " TB I/698 "
—, experimental tuberculosis and, 126
— in tuberculosis of children, 437
— — —, pulmonary, 437
— — —, surgical, 436
Thiopentone anaesthesia, carbohydrate and protein metabolism and, 121
— in extrapyramidal syndromes, 202
Thiouracil, atherosclerosis produced by, 163
—, blood and bone marrow and, 273
— compounds, antithyroid activity, 640
—, gastric secretion and, 182
— in experimental polyarthritis, 87
— — juvenile thyrotoxicosis, 506
— — thyrotoxic auricular fibrillation, 57
— — thyrotoxicosis, liver damage after, 506
—, ovarian function and, 640
— with iodide, 640
Thiourea, blood and bone marrow and, 273
—, toxic effects, 582
Thompson, Ashburton, and the plague, 672*
Thoracoplasty, homolateral, effect of paralysed hemidiaphragm on, 434
— in pulmonary tuberculosis, 434
—, late relapse in collapsed zone of lung after, 214
Thorotrast, late injuries from, 587
Throat, bacterial flora, streptomycin and, 22
Thrombo-angiitis obliterans diagnosis, phlebitis and, 623
— —, hypoglycaemia in treatment, 375
Thrombocytopen in tissues and urine, test for, 475
Thrombocytopenia and increased capillary fragility in liver disease, 168
— in " sedormid " purpura, 498
Thrombo-embolism, blood platelet changes in, 490
—, heparin tolerance test for, 251
Thrombophlebitis migrans, visceral, 61
—, postoperative blood coagulation in, 251
Thrombosis, cerebral, factors affecting prognosis, 527
—, —, stellate ganglion block in, 652
—, coronary artery, blood cholesterol content, 619
—, generalized blood platelet, 274
— of internal carotid artery, 653
— — intracranial veins, 309
—, non-traumatic, of carotid artery, 652
—, venous, anticoagulants in, 61
Thrombus, fibrin and endothelial-cell, acronecrosis due to, 374
— formation, modern concepts of, 490
Thymidine in pernicious anaemia, 165
Thymus shadows, abnormal, artificial anterior pneumomediastinum and, 590
Thyroid, 74–6, 182–3, 291–3, 506–8, 640–1
— carcinoma, radioiodine in, 588
—, compensatory hypertrophy of kidney after nephrectomy and, 75
— deficiency, coeliac syndrome and, 47
— —, excitability of peripheral nerves and, 75
— —, induced, effect on responsiveness to gonadotrophins, 75
— —, skin lesions and, 78
—, desiccated, in cholesterol-induced atherosclerosis, 163
— function, radioactive iodine in measurement, 396
— —, relation of " tridine " to, 506
— iodine utilization, effect of the iodide ion on, 506
—, organic binding of iodine by, 293
Thyroidectomy in experimental polyarthritis, 87
Thyroiditis, subacute, treatment, 396
Thyrotoxicosis, auricular fibrillation in, thiouracil in, 57
—, basal metabolism in, " diparcol " and, 346
— diagnosis, urinary excretion of radioactive iodine in, 396, 397
—, extracellular fluid in, 396
—, glucose tolerance tests in, 74
— in children, propylthiouracil in, 640
— — old age, 641
—, induced, effect on responsiveness to gonadotrophins, 75
—, iodothiouracil, thiocytosine, and (Ca)-4-*n*-propyl-6-oxypyrimidyl-2-mercaptoacetic acid treatments, 293
—, juvenile, thiouracil and, 506
—, mercury poisoning and, 23
—, propylthiouracil in, 182
—, radioactive iodine in, 507–8
—, seasonal variations in, 640
Thyrotoxicosis, serum level of protein-bound radioactive iodine in diagnosis, 74
—, thiouracil treatment, liver damage after, 506
Thyrotropin and thiocyanate, effects on organic binding of iodine by thyroid, 293
Thyroxine antagonist, benzoic acid as, 75
— in myxoedema, 641
Tick-bite fever, aureomycin in, 132
Tinea capitis, manual epilation in, 399
— —, treatment, 297
Tissue changes in total body irradiation, 469
— temperature in resting human forearm, 456
Tobacco addiction, early literature on, 336*
— smoking, pulmonary carcinoma and, 632
Tocopherol, blood level of, in cardiac patients, 157
" Tolserol ", *see* " Myanesin "
Tomatin, *Histoplasma capsulatum* inhibited by, 209
Tomogram of normal vertebrae, 245
Tomography in bladder examination, 592
— — bronchial carcinoma, 139
— — pulmonary tuberculosis, 357
— — tuberculous spondylitis, 592
— — vertebral arthritis, 245
—, pneumoperitoneum and, in investigation of intraperitoneal and retroperitoneal viscera, 592
Tonsillitis, acute, antistreptolysin titre in, 334
—, necrotizing, due to nitrogen mustard, 22
Torticollis, spasmodic, physiological analysis, 314
Torulosis, *see* Cryptococcosis
Toxicology, 22–3, 133–5, 239, 352–4, 462–5, 581–4
—, **industrial,** 23–4, 239–41
Toxoplasmosis, congenital, 478
—, —, sulphadiazine and antiserum in mice, 220
—, human, serological diagnosis, 146
—, laboratory diagnosis, 476*
Trachea, congenital obstruction, 255
—, tuberculosis of, 547
Traumatology in Ancient Egypt, 2800 B.C., 112*
Trench fever, laboratory infections, relation to epidemiology, 98
Trendelenburg position, historical notes on, 559
Treponema immobilization test of normal and syphilitic sera, 513
— *pallidum*, aureomycin and, 303
— —, cultivation, 302
Trichophytin, urticarial reactions to, 79
" Tridine ", thyroid function and, 506
" Tridione " in minor epilepsy, 205, 312, 530
Triethylene glycol in air disinfection, 561
— —, bactericidal action, 561
Trihexyphenidyl, *see* " Artane "
Trimethylammonium group in acetylcholine, specificity of, 124
Trimethylenetrinitroamine poisoning, epileptic attacks in, 23
" Tromexan ", *see* " Pelentan "
Trotter, Thomas, 1760–1832, 336*

Trypanosoma cruzi, incidence in *Triatoma* in Texas, 331
Trypanosomiasis control, planning of, 226
Tsutsugamushi disease, chloramphenicol in, 320, 421
— —, immunity in guinea-pigs, 98
Tubercle bacillus, *see Mycobacterium tuberculosis*
Tuberculin allergy in streptomycin - treated tuberculosis, 430
— from B.C.G. cultures, 101
— hypersensitivity, cutaneous, cellular transfer of, 364
—, leukergy production by, as test of tuberculosis activity, 363
— patch test, modifications, 426
—, P.P.D., in non-pulmonary tuberculosis, 326
— test in children, 562
— — — streptomycin - treated tuberculous meningitis, 433
Tuberculosis, 101–5, 214–19, 325–30, 425–38, 547–56, 663–9
— activity, leukergy production by tuberculin as test of, 363
—, *p*-aminobenzoic acid in, 438
—, aortic, haematogenous tuberculosis and, 426
—, antihistaminic drugs in, 215
— bacillus, *see Mycobacterium*
—, bronchial, 547, 555
—, —, diagnosis and treatment, 426
—, coccidioidomycosis, disseminated, associated with, 417
—, cutaneous, calciferol in, 188
—, —, streptomycin in, 511
—, dihydrostreptomycin in, 664
—, experimental, *p*-aminosalicylic acid in, 437
—, —, cosmic radiation in, 34
—, —, high altitude and, 34
—, —, thiosemicarbazone in, 126
— infection from dogs, 425
— in children, cardiac changes in, 247
— — —, streptomycin in, 328, 665
— — —, — —, abuse of, 328
— — Europe during and after World War II, 547
— — Indonesians, 325, 428
— — liver and spleen, radiographic picture, 246
— — nurses, 15-year follow-up study, 428
—, laryngeal, TB I/698 E therapy, 549
—, lymphohaematogenous, and disseminated coccidioidomycosis, 109
—, mass radiography in, follow-up study, 426
—, miliary, liver biopsy in, 429
—, —, self-induced, 665
—, —, streptomycin in, 430
—, —, — and " promizole " in, 217
— mortality in childhood, 114
—, " neohetramine " in, 215
—, non-pulmonary, P.P.D. treatment, 326
—, —, thiosemicarbazone in, 436
—, pulmonary, *p*-aminosalicylic acid in, 217, 218, 667
—, —, artificial pneumothorax in, 103
—, —, bronchial lavage in, 554
—, —, bronchogenic carcinoma associated with, 175
—, —, — seeding and spread, 435
—, —, *Candida* in sputum from, 363
—, —, cavernous, TB I and TB IV treatment, 436
—, —, cavitation in apex of lower lobe in, 214
—, —, —, development of streptomycin-resistant *Myco. tuberculosis* and, 433
Tuberculosis, pulmonary, cavitation, elastic, specific allergic theory of, 547
—, —, —, prognosis of healed, 547
—, —, —, spontaneous healing of, 669
—, —, in children, streptomycin in, 433
—, —, collapse therapy, 102
—, —, contralateral relapse after unilateral collapse therapy, 325
—, —, " early foci " in, 218
—, —, extrapleural pneumonolysis with " lucite " plombage in, 553
—, —, functional lung segments and signs of neural influence on, 555
—, —, hypoxaemic changes in circulation in, 555
—, —, intradermal streptomycin in, 552
—, —, Klare's scheme and course of, 553
—, —, nitrogen mustard for, 16
—, —, phreniclasis in, 434
—, —, plasma viscosity in, 252
—, —, pneumothorax and phrenicotomy in, interpretation, 553
—, —, posture in treatment, 435
—, —, " promizole " in, 668
—, —, Rasmussen's aneurysms and fatal haemorrhage in, 556*
—, —, relapse in, 101
—, —, secondary intestinal tuberculosis with, *p*-aminosalicylic acid in, 327
—, —, skin–lung reflex in, 554
—, —, streptomycin in, 430, 433
—, —, — and pneumothorax in, 216
—, —, " sulphetrone " in, 552
—, —, " TB I/698 " in, 326, 666
—, —, thiosemicarbazone, intracavernous, in, 437
—, —, thoracoplasty in, 434
—, —, tomography in, 357
—, rehabilitation and resettlement in, 449
—, renal, pulmonary and urogenital tuberculosis in pathogenesis, 435
— resistance, role of protein in, 214
—, skin, vitamin D treatment, 644
— specialist, V. A. Manassein, 336*
—, streptomycin in, mechanism of action, 215
—, — —, 400 cases, 216
—, —, treated, tuberculin allergy and erythrocyte sedimentation rate in, 430
—, sulphones and streptomycin in, 328
—, " TB I/698 " in, 102, 549, 550
—, thiosemicarbazone in, toxic effects in children, 437
—, tracheal and bronchial, 547
—, urinary tract, *p*-aminosalicylic acid and streptomycin in, 328
—, urogenital, streptomycin in, 551
— vaccination with murine type of tubercle bacillus, 3
Tubocurarine, dimethyl-, and regulation of blood pressure, 15
— iodide, dimethyl ether of, pharmacology, 125
— in oil–wax suspension in rheumatoid spondylitis, 86
Tularaemia, aureomycin in, 324, 546
—, experimental, polymyxin in, 662
— in Paris, 663
—, morbid anatomy and histology, 474
—, streptomycin in, 424
Tularaemia transmission in Arkansas, changing picture of, 4
Tumour identification, heterologous bio-cytoculture for, 248
—, mouse, propagation by dried tissue, 247
— tissue, water movement in, 142
—, vesical, in workers in chemical industry, 6
Tungsten poisoning, BAL in, 240
Typhoid, aureomycin and chloramphenicol in, 131
— carriers, chloramphenicol in, 543, 660
— —, penicillin–sulphathiazole treatment, 544
— —, protective measures against, 226
—, chloramphenicol in, 237, 321, 322, 422, 543, 544
—, encephalitic, chloramphenicol in, 349
— infection of ovarian cysts, 321
— vaccine, renal manifestations of glomerulonephritis and, 195
Typhus, *p*-aminobenzoic acid in, 543
—, epidemic, in south-western Arabia, 114
—, exanthematous, aureomycin in, 320
—, haematopoietic system in, analysis of changes in, 321
—, laboratory infections, relation to epidemiology, 98
—, murine, vaccination, antibody response to, 97
—, scrub, *see* Tsutsugamushi disease
— vaccine, effect on rickettsiae in body lice, 98
Tyrosine metabolism in scurvy 487
" Tyrosolvin ", antibacterial action *in vitro*, 349

Ulcer, duodenal, casein hydrolysate, milk, and milk-cream effect, 286
—, —, in infants, 607
—, —, sodium carboxymethylcellulose as antacid in management of, 391
—, gastric; benign, nocturnal gastric secretion in, 71
—, —, chronic, nitrogen mustard in, 636
—, —, differential diagnosis from carcinoma, 31
—, —, duodenal and, early descriptions, 559*
—, —, — —, prolonged mecholyl producing, 285
—, —, experimental production 503
—, —, in old age, 636
—, —, stomach shape, significance of, 473
—, —, synthetic resins in, 392
—, gastroduodenal, bismuth in, 503
—, leg, arteriosclerosis obliterans as cause of, 622
—, —, gravitational, 295
—, mouth, local aureomycin in, 390
—, peptic, acidity in pathogenesis, 286
—, —, antipeptic and antacid therapy, 176
—, —, chronic, haematemesis in, 70
—, —, —, nitrogen balance in, 286
—, —, glucose tolerance in, 176
—, —, in childhood, 482
—, —, — factory workers, 115
—, —, indications for gastrectomy in, 637
—, —, medical treatment, follow-up study, 176
Ulcer, peptic, narcosis, prolonged, in treatment, 392
—, —, neuro-hormonal factors in pathogenesis, 636
—, —, oesophageal, 283
—, —, recurrence, entero-gastrone and, 70
Ultrasonic waves, therapeutic applications, 585
Ultraviolet irradiation, anatomical and physiological effects, 597
Undecylenic acid in psoriasis, 189
Undulant fever, *see* Brucellosis
Uraemia, anuric, conservative treatment, 304
—, artificial kidney, peritoneal lavage, and other methods of treatment compared, 83
—, diet and hormonal influences in, 195
—, enteric perfusions with hypotonic solutions in, 304
—, hyperpotassaemia and electrocardiographic changes in, 404
Uranium poisoning, amino-aciduria in, 133
— —, BAL in, 240
Urea clearance, significance, 602
— — tests, 601
—, hypertonic solution, renal response, 231
Urethane derivatives, relation between chemical structure and antileukaemic action, 66
—, effect on division of fibroblasts, 35
— in chronic myeloid leukaemia, neutropenia, and thrombocytopenia after, 169
— — leukaemia, 30
— — multiple myelomatosis, 170
Urethritis, acute gonorrhoeal, chloramphenicol in, 402
—, non-specific gonococcal, aureomycin in, 402
—, — —, in soldiers, 300
Uric acid metabolism in normal and gouty subjects, 488
Urinary tract infection, *Aerobacter aerogenes* causing, aureomycin in, 647
— — —, oral aureomycin in, 647
Urine analysis, " glass-tube method ", 602
— incontinence, " diaparene " in, 398
— phenol fractions in pernicious anaemia, effect of vitamin B_{12} on, 626
Urography, intravenous, in bladder tumour assessment, 358
Urticaria, solar, 187
Uterus, cervix, carcinoma, radium treatment, complications, 245
—, radiological picture in relation to function, 32

Vaccination, smallpox, *see* Smallpox vaccination
—, tuberculosis, with murine type of tubercle bacillus, 3
—, typhus, murine, antibody response to, 97
Vaccinia infection in cattle, 657
— virus, heated penicillin and, 603
— — infection in children with atopic dermatitis, 78
Vagotomy, immediate and late results, 391
— for peptic ulcer, gastric mucosa appearance, 287
—, psychiatric aspects 287
Val-de-Grace, military hospital of, 560*
Vanadium poisoning BAL in 240

Van Buren, William H., New York physician in nineteenth century, 112*
" Vanishing cream ", effect on skin of " carbitol " in, 186
Vaquez–Osler's disease, 170
Vascular diseases, deoxycortone and anterior pituitary preparation causing, 475
— —, peripheral, iontophoresis in, 271
— —, —, tetraethylammonium bromide in, 379
— —, —, — chloride in, 271
Vas deferens, ligation, late effects of, 8
Vasomotor tone, effect of tetraethylammonium salts on, 268
Vegetable gums, allergic disorders and, 259
Veins, intracranial, thrombosis of, 309
— of leg, function of, 163
—, portal, obstruction, diagnosis by intestinal absorption of glucose, 390
—, pulmonary, aberrant insertion associated with interatrial septal defect, 356
—, —, right, anomaly diagnosed during life, 266
Vena cava, superior, obstruction, 162
— —, —, —, in primary carcinoma of lung, 389
Venereal diseases, 82, 191–4, 300–3, 400–2, 513–16, 645–6
— —, circumcision and, 300
— —, social history and advertisements on treatment, 224*
Veratrum viride, chemical fractions, assay in man, 573
— —, effect on essential hypertension, 161
" Veriloid ", hypotensive extract from veratrum viride, 271
Verrucosis, generalized, epidermodysplasia verruciformis and, 298
Vertebrae, closed fractures, nervous sequelae, role of segmental arachnoiditis in, 203
Vertebrae, diseases of, tomography in, 245
—, tomograms of normal, 245
—, upper cervical, non-pathological variations in, 358
Vesalius's *Fabrica* and imitative works, anatomical tabulae and initial letters in, 336*
Vestibular apparatus, toxic effect of streptomycin on, 130
Vibratory tools, Raynaud's phenomenon in workers with, 227
" Vigantol ", *see* Calciferol
Virus infections, 95–7, 209–11, 318–20, 418–19, 537–40, 657–9
— infectivity, neutralization by thermolabile component of serum, 477
— (JHM), isolation, biological properties, and pathology, 477
—, thermolabile component of serum combining with, 477
Visammin, coronary vasodilator action, 56
— treatment of pertussis, 661
Viscera, intra- and retroperitoneal, tomography with pneumoperitoneum in investigation of, 592
Vitamin A absorption in sprue, 178
— — deficiency, skin lesions associated with, 78
— — in hypertension, 270
— — — ichthyosis, 644
— — — origin and prophylaxis of amyloidosis, 474
— — — tuberculous meningitis, 432
— B complex, synthetic, in glossitis of Addisonian pernicious anaemia, 276
— — excretion in diabetes, 373
— B_1, *see* Aneurin
— B_2, *see* Riboflavin
— B_{12}, effect on urinary phenol fractions in pernicious anaemia, 626
— — in combined degeneration of spinal cord in pernicious anaemia, 412
Vitamin B_{12} in megaloblastic anaemia of infancy, 626
— — — pernicious anaemia, 626
— — — — —, resistance, 627
— — — — and nutritional macrocytic anaemia and sprue, 276
— — — subacute combined degeneration of spinal cord, 525
— — — tropical sprue in relapse, 486
— C deficiency in diets of Sudanese village, 488
— — metabolism, effect of calcium ascorbate on, 232
— D, " promanide " and, in tuberculoid leprosy, 543
— — in skin tuberculosis, 644
— — therapy, toxic effects, 189
— D_2, *see* Calciferol
— E deficiency, abruptio placentae in, 119
— — in diabetes mellitus, 489
— therapy in allergic conditions, 151
Volvulus, gastric, in infants, radiology of, 591
Vomiting, cyclical, in infancy, 482

War neuroses of children, 484
Ward, Frederick Oldfield, pioneer of osteogeny, 560*
Warts, podophyllum resin in, 81
Water deprivation, renal haemodynamics and, 120
— exchange after blood transfusion, 466
— hemlock, poisoning by, 583
— movement in normal and tumour tissues removed from body, 142
— and salt distribution in heavy sweating, 7
— — — intake, prickly heat and, 295
Waterhouse, Benjamin, and introduction of vaccination into United States, 112*
Weight increase in infants after B.C.G. vaccination, 337
Weil's disease in north-east Scotland, 340
Wheat germ in infant feeding, 46
Whitlows, *x*-ray treatment, 243
Whooping-cough, *see* Pertussis
Wilson's disease, carbohydrate metabolism disturbances in, 203
— —, postero - lateral column degeneration and, 310
Withering, William, 560*
" Win 1011 " and " Win 246 ", effect on *Entamoeba*, 440
Wolff–Parkinson–White syndrome with paroxysmal AV-nodal tachycardia, haemodynamic studies of, 158
Wound healing, cortisone and, 643
Wry-neck, *see* Torticollis

Xanthopterin, effect on haematopoiesis and growth in rats, 66
X-ray irradiation, heart and circulation and, 468
— — injuries of bladder and rectum, 470
— — — —, foetal, 243
— —, natural resistance to infection in rheumatoid arthritis and, 587
— —, wide-field, platelet count in control of, 589
— —, *see also* Radiotherapy
" Xylocain ", isomers and homologues of, pharmacological properties, 458

Yellow fever at Boa Vista, 559*
— —, sylvan, outbreak in Uganda, 96

Zinc content of erythrocytes, relation to carbonic anhydrase activity, 63
— — — whole blood, plasma, leucocytes, and erythrocytes in anaemias, 63

AUTHOR INDEX TO VOLUME 7

JANUARY—JUNE 1950

References are to page numbers. An asterisk denotes title and reference only

AANONSEN, A., 325
AAS, K., 123, 375
ABAZA, A., 649
ABBOTT, L. D., 626
ABBOTT, O. A., 594*
ABDEL KADER, M. M., 119*
ABEATICI, S., 355
ABELL, R. G., 575
ABERNETHY, T. J., 562, 603
ABOLINS, J. A., 358
ABRAHAM, E. P., 579*
ABRAHAMS, D. G., 333, 537
ABRAMSON, H. A., 49
ABUL-FADL, M. A. M., 567*
ACHESON, G. H., 11, 572
ACKERMAN, L. B., 556*
ACKROYD, J. F., 7, 66, 497, 498
ADAMS, A. R. D., 443
ADAMS, E. B., 277
ADAMS, E. E., 397
ADAMS, F. H., 364*
ADAMS, G. D., 138
ADAMS, J. E., 91
ADAMS, J. M., 364*
ADAMS, R. D., 92, 257
ADAMSON, C. A., 145*
ADAMSON, J. D., 450
ADELSBERGER, L., 430
ADLER, D. K., 127
AFANASEVA, V. M., 247
AGATE, J. N., 227, 467
AGNEW, L. R. C., 45*
AGRESS, C. M., 183*, 374
AHRENS, E. H., 504
AIDAR, O., 569
AIKAWA, J. K., 147
AITKEN, G. A., 23*
AITOFF, V., 584
AKIMOVA, V. V., 253
AKRAWI, F., 301
ALAIN, M., 100
ALBERT, A., 291, 294
ALBIN, M. B., 423
ALBOU, A., 349
ALBRIGHT, F., 51
ALDMAN, B., 77
ALDRIDGE, A. O., 224*
ALDRIDGE, W. N., 464
ALEKSANDROWICZ, J., 16, 65
ALEXANDER, B., 142*
ALEXANDER, F., 160
ALEXANDER, H., 555
ALEXANDER, H. E., 145
ALEXANDER, L. J., 301, 515
ALEXANDER, S. B., 293
ALEXANDER, W. R. M., 648
ALFORD, W. C., 341, 464*
ALIMURUNG, M. M., 490
ALLANBY, K. D., 59, 493
ALLARD, —., 431
ALLEN, D. I., 8
ALLEN, F. H., 497
ALLEN, J. G., 587*
ALLEN, R. M., 532
ALLEN, T. C., 236
ALLIOT, M., 206
ALLISON, A., 506
ALLSOPP, C. B., 36*
ALMY, G. M., 138
ALTMANN, R., 591
ALTON, O. M., 135
ALTSCHULE, M. D., 63
ALVAREZ SÁINZ DE AJA, E., 189
ALVAREZ, W. C., 316
ALWALL, N., 197*
ALZAMORA-CASTRO, V., 54
AMBACHE, N., 9*
AMELI, N. O., 652
AMICI, R., 242
AMILL, L. A., 665
AMOUSSOU,—., 208
AMSTERDAM, S. D., 446
AMYES, E. W., 652
ANANENKO, E., 126
ANASTASOPOULOS, G., 584
ANDERSEN, D. A., 329
ANDERSEN, D. H., 150
ANDERSEN, H. A., 38
ANDERSEN, P. E., 589
ANDERSON, D., 438
ANDERSON, E., 643
ANDERSON, H. H., 440
ANDERSON, P. M., 329*
ANDERSON, S. G., 95
ANDRÉ, M. J., 464
ANDREANI, G., 308
ANDREAS, E., 171
ANDREOLA, E., 87
ANDREWS, C. T., 384
ANDREWS, G. W. S., 127
ANDRINI, F., 330*
ANGHELESCO, A., 118*
ANNING, S. T., 295
ANREP, G. V., 56
ANSON, B. J., 336*
ANTONI, H. N., 598
ANTUNES, A., 511
ANTZ, H., 308
APGAR, V., 233*
APPEL, M., 68
APPELBAUM, E., 423
APPELGREN, A., 520
APRÀ, A. A., 190*
AP SIMON, D. J., 562
APT, L., 353
APTER, L., 256
ARAMBURU, T., 166, 276, 411
ARBUCKLE, R. K., 139
ARCADI, J. A., 517
ARENSON, N., 608
ARIEFF, A. J., 318
ARJONA, E., 144
ARKADYEVSKII, A. A., 566
ARMEN, R. N., 155
ARMSTRONG, B. W., 361*
ARMSTRONG, T. G., 106
ARMSTRONG, W. C., 429*
ARNDT, T., 549*
ARNOLD, O. H., 535
ARNOLD, P., 271, 272
ARNOLD, R. C., 645
ARNOTT, D. G., 397
ARNOTT, W. M., 259
ARONOFF, S., 61*
ARRECHE, C. C., 446
ARRIAGA CANTULLREA, J., 560*
ARRIAGADA, A., 461, 579*
ARRUDA, E., 584*
ASHBY, D. W., 652
ASHBY, W. R., 536
ASHEN-BRUCKER, H., 383
ASHER, R., 292
ASHFORD, C. A., 177
ASKEY, J. M., 57
ASPIN, J., 426
ASTWOOD, E. B., 76*
AUB, J. C., 6*
AUDOYE, —., 663
AUERBACH, O., 547, 599
AUERSPERG, A., 569
AUERSWALD, W., 317
AUSTIN, G., 410
AUSTIN, G. M., 160
AUSTIN, V. T., 138
AUTERA, L., 270
AUZEPY, P., 328
D'AVIGNON, M., 496
AXELROD, A. R., 164
AYKROYD, W. R., 1
AYRES, S., 80
AYVAZIAN, L. F., 428
AZAR, J. E., 332
AZULAY, R. D., 511
AZZOPARDI, P. G., 68
BABAYANTS, R. A., 562
BABKIN, B. P., 567*
BACH, F., 86*
BACHMAN, A. L., 244
BACKER, M., 118*
BACON, E. K., 345*
BACON, H. E., 254*
BACQ, Z. M., 156
BADER, R. A., 182
BADGER, G. F., 562, 603
BADGER, T. L., 428
BADOSA-GASPAR, J., 635
BADRICK, F. E., 396
BAER, H., 567
BAER, R. L., 189
BAER-HESS, V., 654
BAGNALL, D. J. T., 453, 566
BAHN, R. C., 638
BAILEY, C. A., 402
BAILEY, O. T., 477
BAILEY, R., 337
BAIN, W. A., 49
BAIRD, J. W., 537
BAIRD, M. E., 352
BAKER, A. B., 308
BAKER, A. H., 301
BAKER, C., 67
BAKER, L. A., 261*
BAKKE, J. L., 89
BALABAN, M., 137
BALDI, G., 24
BALDRIDGE, G. D., 578
BALDUINI, M., 616*
BALDWIN, D. S., 195
BALDWIN, E. DE F., 173
BALI, T., 249*
BALL, K. P., 61
BALLANTINE, H. T., 268
BALTHAZARD, V., 27
BANERJEE, D., 322*
BANFIELD, W. G., 578
BANG, H. C., 40, 494
BANKER, D. D., 544
BARACH, A. L., 328*
BARAÑAO, A., 249
BARANOV, V. G., 112, 270
BARBER, M., 42, 253
BARBERI, S., 332*
BARBIERI, L. L., 80
BARCROFT, H., 163, 575
BARER, A. P., 64*
BARGEN, J. A., 393
BARIATTI, R., 182
BARIBEAU, B. J., 45*
BARILYAK, R. A., 143
BARKER, H. G., 574
BARKER, L. P., 656
BARKER, P. S., 159
BARLOW, C. H., 221
BARNES, A. R., 110
BARNES, E. M., 18
BARNES, J., 672
BARNES, J. M., 464
BARNES, Z. B., 546
BARONI, V., 551*, 669
BARR, M., 45*, 563
BARRERA, S. E., 317
BARRETT, R. H., 581
BARRON, S. S., 359
BARSOTTI, M., 23, 116
BARSOUM, G. S., 56
BARTA, L., 484*
BARTELS, C. C., 60
BARTELS, E. C., 641
BARTELS, H. L. J. M., 64
BARTON, H. C., 39
BARTON, R. L., 302
BARWELL, C. F., 600
BASTIN, R., 328
BASNUEVO, J. G., 444
BASS, D. E., 182
BASS, H. E., 172
BASSET, A., 135*
BAST, T. H., 112
BASTIEN, J., 160
BASTRUP-MADSEN, P., 35
BATSON, H. C., 605
BATTERMAN, R. C., 85, 233
BATTIGALLI, O., 330*
BATTILANA, G., 54
BATTISTINI, G., 44
BATTLE, W. D., 576
BATTY, I., 146
BAUER, D. J., 477*
BAUER, E. G., 290
BAUER, F. C., 230*
BAUER, R., 589
BAUER, T. J., 302
BAYAN, A. P., 43
BAYLES, T. B., 518
BAYLISS, R. I. S., 618
BAZ, I. I., 537*
BAZETT, H. C., 455
BEADLES, J. R., 568
BEAKEY, J. F., 279, 499
BEAL, G. A., 663
BEARD, E. E., 405
BEARD, J. W., 562, 603
BEARDSLEY, F. A., 104, 105
BEARE, J. M., 80
BEATTIE, E. J., 631*
BEATTY, J. O., 580
BEAUVILLAIN, A., 241
BECHGAARD, P., 83, 381, 494
BECK, I. T., 14
BECK, V., 636
BECKER, A. M., 463
BECKER, F. R., 547
BECKER, J., 460
BECKER, T. J., 126
BECKMANN, G. E., 193
BECQUET, R., 287*
BEDSON, S. P., 600
BEDÜRFTIG, G., 468
BEECHER, H. K., 571
BEEKMAN, F., 560*
BEEKMAN, R. S., 176
BEELER, J. W., 242
BEERSTECHER, E., 152
BEET, E. A., 496
BEGLIN, N., 346
BEHRMAN, H. T., 186
BEIGELMAN, P. M., 425, 461*
BEITMAN, M. R., 581
BEKKEROV, G. E., 78
BELER, B., 22
BELINSON, L., 524
BELL, E. J., 656
BELL, J. A., 19, 465
BELLET, S., 262
BELLONI, L., 559
BELTON, F. C., 579*
BENCHIMOL, A. B., 616
BENDA, C. E., 311
BENDA, R., 105*
BENDEL, W. L., 295*
BENDER, L., 207
BENDITT, E. P., 367*
BENEDEK, T., 109*
BENEDICT, J. D., 488
BENEDICT, R. B., 458*
BENEFIELD, U. R., 658
BENHAMOU, E., 191, 349, 495, 542
BENJAMIN, Z. H., 155
BENNETT, H. J., 445*
BENSLEY, E. H., 489
BENSON, E. S., 417
BENTLEY, G., 570
BERARD, L., 551
BERBERIAN, D. A., 331, 440
BERESTON, E. S., 189
BERG, K., 130
BERGAMASCO, A., 297
BERGER, E. Y., 196
BERGMAN, H. C., 183*, 378

BERGNER, A. D., 577
BERGSTRAND, A., 83
BERINGER, A., 359
BERISH, H., 489
BERK, J. E., 286
BERK, L., 348
BERKE, H., 133
BERKE, R., 172
BERKOS, K. P., 2
BERMAN, A. B., 508*
BERMAN, J. K., 272
BERMAN, L., 164
BERNAL, P., 378
BERNARD, E., 430, 431
BERNARD, J., 135*, 387
BERNARDIN, R. M., 422
BERNIER, G., 106
BERNIER, J. J., 84
BERNOU, A., 214, 429, 547
BERNSTEIN, A., 571
BERNSTEIN, L., 156
BERNSTEIN, T. B., 50*
BERNT, H., 462*
BERRY, J. W., 254
BERRY, L. J., 152
BERRYMAN, G. H., 568
BERTHRONG, M., 77*
BERTO, R., 661
BERTOLI, R., 656*
BERTOZZI, P., 5*
BERTRAND, G., 438
BERTRAND, I., 309*, 570, 651*
BERTRAND, L., 429, 543, 600*
BESKOW, A., 667
BESSEIGE, H., 106
BESSEY, O. A., 454
BESSIS, M., 164, 167, 466
BEST, C. H., 595
BETHELL, F. H., 165
BETTLEY, F. R., 78
BEVANS, M., 163
BHAGVAT, K., 52*
BHATTACHARYA, B. K., 328
BHENDE, Y. M., 626
BICKEL, G., 354
BICKERS, D. S., 257
BIDWELL, E., 144
BIGGART, J. H., 560*
BIGGER, J. W., 544
BILIBIN, A. F., 324
BILLINGS, F. T., 390
BILLINGS, J. H., 172
BINDER, M. L., 538*
BINE, R., 572
BINET, L., 658*
BING, R. J., 58, 157
BIONDINI, B. A., 430
BIÖRCK, G., 379
BIRGE, R. F., 168
BIRKHILL, F. R., 465
BIRKNER, R., 30, 587
BISCHOFF, H., 423, 462*
BISHOP, E. A., 606
BISHOP, L. W. J., 600
BISHOP, W. J., 336*
BLACK, M. B., 289
BLACK-SCHAFFER, B., 474*
BLACKWELL, U., 48
BLADES, B., 631*
BLAICH, W., 351
BLAKE, W. D., 36
BLANC, F., 108
BLANC, H., 258
BLANCHE, J. A., 551
BLAND, C., 572
BLANEY, L. F., 242
BLANK, H., 578
BLATCHLEY, E. D., 579*
BLEGEN, E., 123, 375
BLICHARSKI, J., 16, 65
BLISS, W. R., 602
BLOCK, M. H., 81, 170, 385
BLOMFIELD, A. M., 478
BLONDHEIM, S. H., 504
BLOOM, D., 190
BLOOM, M. L., 167
BLOOM, W. L., 372
BLOXSOM, A., 319*
BLUHM, I., 225
BLUMENFELD, H., 172
BLUNT, J. W., 643
BOAK, R. A., 302
BOAND, A., 42
BOBROVA, A. S., 474
BOCCA, E., 178
BOCK, G., 275
BOCK, H. E., 278*
BOCKUS, H. L., 286, 288
BÖE, J., 44*, 113
BOELES, J. T. F., 75
BOELTER, M., 235
BOENJAMIN, R., 543*, 659
BOGDANOVIĆ, M., 435
BOGDATYAN, M. G., 223
BOGER, W. P., 20, 129, 580
BOHAN, K. E., 58
BOHNHOFF, M., 22
BOHNSTEDT, R. M., 582
BOIKAN, W. S., 233
BOLAND, E. W., 407
BOLDREY, E., 91
BOMMELAER, M., 593
BONDY, P. K., 372
BONHOFF, G., 311
BONI, A., 406
BOOKER, W. M., 121
BOONE, B. R., 594*
BOOTS, R. H., 521
BOQUIEN, Y., 537*
BORAK, J., 81
BORDEN, C. W., 263
BORECKA, D., 363
BORGES, S., 621
BORNE, S., 78
BORNSCHEIN, H., 317
BORTH, R., 291*
BOSHES, B., 318
BOSSI, C., 169
BOSTICK, W., 440
BOUCHARD, J., 470
BOURNE, G., 570
BOURNE, W. A., 69, 374*
BOUSFIELD, G., 225
BOUSSER, J., 384
BOVENTER, K., 25
BOVET, D., 352
BOWDEN, K. M., 26
BOWERS, R. E., 299
BOWLEY, C. C., 343*
BOYD, D. A., 92
BOYD, F. J., 272
BOYD, M. F., 107
BOYD, W. L., 450*
BOYETTE, D. P., 367*
BOYLE, A. C., 585
BOYLSTON, G. A., 504*
BRADBURY, J. T., 594
BRADFORD, W. L., 423*
BRADLEY, R., 399
BRAGIN, M. S., 79
BRAID, F., 324
BRAIER, L., 135*
BRAIN, R. T., 297
BRAIN, W. R., 311
BRAINERD, H., 238
BRAMS, W. A., 264
BRANDT, M., 630
BRAS, G., 209
BRASS, K., 401
BRATTON, A. B., 319
BRAUDE, A. I., 662
BRAUN, H. A., 240
BRAUNSTEINER, H., 568*
BRECKENBRIDGE, R. L., 358
BREDMOSE, G. V., 609
BRENDLER, S. J., 9*
BRENN, H., 89
BRESLER, R. R., 227
BRESNICK, E., 279, 486
BRET, J., 219*
BRETON, A., 554
BRETT, R., 644
BREU, W., 154
BREWIS, E. G., 95
BREWSTER, J. M., 539
BRICK, I. B., 391
BRICKA, M., 164
BRIEGER, E. M., 556*
BRIERLEY, J. B., 9*
BRINDLE, H., 462*
BRINEY, A. K., 110*
BRISSAUD, H. E., 479
BRITO E CUNHA, J. L., 138
BROADBENT, J. L., 49
BROADBENT, T. R., 129
BROAGER, B., 650
BROCH, O. J., 84, 158
BRØCHNER-MORTENSEN, K., 522
BROCKBANK, W., 112*, 448*
BROCKMAN, L., 263
BROD, J., 404
BRONK, T. T., 68
BROOKE, B. N., 637
BROOKS, A. M., 376
BROOKS, C. McC., 574
BROOM, J. C., 209
BROSER, K., 534
BROTHERS, M. J., 460
BROUWER, B., 257
BROWN, A., 171, 276, 288
BROWN, B. B., 460*
BROWN, G. E., 345
BROWN, H. W., 91, 136, 321*, 664
BROWN, M., 318
BROWN, R. K., 62
BROWN, T., McP., 405
BROWN, W. E., 594
BROWNSON, B. C., 71*
BROŽEK, J., 611
BRUCH, H., 257
BRUCK, E., 404*
BRÜCKE, F. V., 59
BRÜGGEMANN, W., 65*
BRÜGGER, Y., 521
BRUGER, M., 39
BRULÉ, G., 177
BRUN, C., 195
BRUNAUER, S. R., 80
BRUNEL, D., 551*
BRUNETTI, O., 145
VON BRUNN, W. L., 525
BRUSA, P., 82
BRUUN, E., 260
BRUYER, —., 135*
BRUYN, H. B., 238
BRYAN, C. E., 66
BRYAN, R. S., 249
BRYER, M. S., 238, 461
BRYSON, V., 664
BRZEZINSKY, A., 20, 362
BUBB, W., 376
BUBIS, S., 280
BUCHANAN, T. J., 585
BUCHBERG, A. S., 330*
BUCHHOLZ, B., 550
BUCHT, H., 250*
BUCK, M., 18
BUCKELL, M., 467
BUDD, E., 486
BUECHLER, E., 165*
BÜCHMANN, P., 658
BÜLBRING, E., 183
BUERK, M. S., 192
BUHOT, S., 64
BUKA, R., 293*
BULL, G. M., 304
BULLOCK, W. K., 633
BUNDESEN, H. N., 515
BUNGE, R., 669*
BUNNER, R., 31
BURCH, G. E., 234*
BURCH, H. B., 454
BURCHELL, H. B., 158, 247
BURCHENAL, J. H., 348
BURCKHARDT, W., 514
BURFORD, T. H., 594*
BÜRGI, S., 309*
BURK, D., 229
BURKE, F. G., 423, 462*, 662
BURKE, J., 580
BURN, J. H., 183
BURNETT, C. H., 51
BURNS, H. A., 668
BURT, C. C., 577
BURTON, H. S., 18*
BUSCHKE, F., 243
BUSSE, W., 56
BUSSON, A., 179
BUTCHER, H. R., 499
BUTTLE, G. A. H., 349
BYERS, S. O., 572
BYROM, F. B., 621

CABRERA, B. D., 446
CACCESE, A., 275
CACCIALANZA, P., 644
CACCURI, S., 117
CACHERA, R., 396
CAFFEY, J., 607
CAHAN, A. M., 486*
CALABI, V., 465*
CALANDI, C., 432
CALCUTT, G., 36*
CALDEYRO, R., 124
CALDWELL, E. R., 239*, 420
CALKINS, E., 250
CALLEN, I. R., 624
CALO, A., 377
CAMELIN, A., 160
CAMERON, D. G., 166
CAMERON, W., 462
CAMINOPETROS, J., 542
CAMMERMEYER, J., 92
CAMPANACCI, D., 348
CAMPBELL, A. M. G., 318
CAMPBELL, D. C., 496
CAMPBELL, J. D., 583
CAMPBELL, M., 492, 493, 560*
CAMPBELL, V. W. H., 300
CAMPI, L., 355
CAÑADELL, J. M., 78, 292
CANALES, P., 43
CANELAS, E. Z., 661
CANELIS, M., 531*
CANET, J., 670
CANETTI, G., 552
CANFIELD, A. A., 345
CANIZARES, O., 260, 369, 657
CANON, R., 51*
CANTRELL, W., 108
CANTRIL, S. T., 243
CAPLAN, P. S., 405
CAPPIO, M., 131
CAPPS, R. B., 39
CAPPS, R. T., 576
CARANDO, Q., 244*
CARD, W. I., 310
CARDULLO, H. M., 46
CAREN, R., 372
CAREY-TREFZER, C., 484
CARLE, B. N., 662
CARLÉ, R., 226
CARLGREN, L. E., 633
CARLINER, P. E., 48, 189
CARMODY, M. G., 340
CARNEIRO, R. D., 616
CARNES, W. H., 387
CAROLI, J., 167, 206
CARPENDER, J. W. J., 169
CARPENTER, C. M., 302
CARR, C. E., 357
CARR, D. T., 126, 296*, 664
CARR, T. L., 251
CARROLL, D. S., 625
CARROLL, G. J., 624
CARSON, M. J., 594*
CARSTENSEN, B., 327, 667
CARTAGENOVA, L., 660
CARTER, A. B., 207
CARTER, J. B., 264
CARTER, R. A., 472
CARTER, S., 651
CARTWRIGHT, G. E., 383
CARVALHAL, S., 621
CARVER, A. E., 239*
CARY, C. A., 568*
CASANOVAS, M., 17*
CASE, J. T., 381
CASSANO, A., 323, 422
CASSEN, B., 137
CASTELLANI, A., 425
CASTILLO DE BONNEVEAUX, S., 14
CASTILLO, J. C., 233*, 458
CASTILLO, J. J., 330*
CASTLE, W. B., 348, 627
CASTLEMAN, B., 241
CATES, J. E., 580
CATHALA, J., 328
CATHCART, R. T., 158, 458
CATHIE, I. A. B., 476*
CATTON, R., 177
CAUGHEY, J. E., 5*
CAUSSADE, L., 258
CAVIGNEAUX, —., 6
CAWLEY, E. P., 292*
CAYLA, —., 431
CAZAL, P., 429
CAZZULLO, C. L., 93
CERONE, M., 426
CERUTTI, P., 298
CHANDLER, C. A., 238
CHANDLER, V. L., 516
CHANDRASHAKER, B., 75

CHANG, A., 543*
CHANG, M. C., 454
CHANG, N. C., 543*
CHANUTIN, A., 361*, 475*
CHAPMAN, C. B., 620*
CHAPMAN, D. W., 378
CHAPMAN, S. S., 424
CHAPPLE, W. H. C., 638
CHAPTAL, J., 551*
CHARLES, —, 6
CHARLIER, R., 11, 156
CHARRIER, J., 179
CHASIS, H., 195
CHASSIN, N., 638
CHAUCHARD, P., 151, 584
CHEEVER, F. S., 477
CHEN, C. H., 191*, 193, 513
CHEN, G., 650*
CHEN, H. H., 222
CHEN, K. K., 125
CHEN, T. T., 441*
CHENG, W. J., 445
CHENNELLS, M., 123
CHERNENKO, E. I., 392
CHERRINGTON, M. E., 157
CHESNEY, A. M., 516*
CHEVARRIA, A. P., 440
CHEYMOL, J., 23
CHHUTTANI, P. N., 368
CHICHE, P., 431
CHIEFFI, M., 161*
CHING LU, W., 129
CHINI, V., 66*
CHINN, H. I., 453*
CHIODI, H., 457
CHIODI, J., 174
CHITTUM, J. R., 347*
CHOLAK, J., 240
CHOR, H., 313
CHREST, C. P., 215
CHRIST, P., 297
CHRISTENSEN, E., 201*
CHRISTENSEN, N. A., 247
CHRISTIAN, J. R., 318
CHRISTIE, R. V., 376, 629
CHRISTOFERSEN, H. R., 599
CHU, I. T., 106*
CHUNG, H. L., 445, 543*
CHUSID, J. G., 588*
CHU WU, C. S., 106*
CHWALLA, G., 517*
CIOFFARI, M. S., 149
CISNEROS, F., 378
CISNEROS, T., 81*
CLAESSON, L., 77
CLARK, B., 345
CLARK, D. E., 397
CLARK, J. K., 574
CLARK, J. W., 193*
CLARK, M., 278
CLARK, M. C., 125
CLARK, R. J., 58
CLARK, W. H., 115, 238
CLARKE, D. H., 394
CLARKE, G. H. V., 644
CLARKE, T. W., 672*
CLAVERO, G., 321
CLAYTON, G. D., 226*
CLEMEDSON, C., 142*
CLOUGH, G. B., 153
COATNEY, G. R., 442, 443, 444, 671
COCHRAN, K. W., 354*
COCHRANE, T., 80
CODE, C. F., 69
CODON, A., 260*
COELHO, R. D., 107
COGGESHALL, L. T., 443
COHEN, M. H., 186
COHEN, S. G., 268, 620*
COHN, C., 52
COHN, M. L., 215
COKE, H., 87, 405
COLE, H. N., 515
COLE, J. W., 274
COLEMAN, V. R., 132
COLLARD, P., 612
COLLEN, M. F., 235
COLLINS, D. H., 405
COLLINS, H. S., 174, 537, 543, 631
COLLINS, S. D., 565*
COLLINS, V. P., 656
COLLINS, W. T., 170
COLQUHOUN, J., 209, 580
COMAN, D. R., 597
COMBES, F. C., 186, 260, 369, 511, 657
COMBIER, C., 543
COMFORT, M. W., 71, 72, 283
COMMONS, R. R., 51
COMREY, A. L., 345
CONCANNON, J. P., 245
CONE, W. V., 470
CONKLIN, W. S., 68
CONLEY, J. E., 585
CONNELL, J. F., 351
CONNELL, W. F., 620
CONRAD, K., 91
CONSOLAZIO, C. F., 568
CONSOLAZIO, F. C., 8
CONSTABLE, K., 414
CONSTANS, —, 663
CONTE, S., 660
CONTI, F., 323, 422
CONTRERAS, F., 81
CONWAY, E. J., 454*
CONWAY, H., 491
COODLEY, E. L., 638
COOK, H. F., 585
COOK, R., 45*
COOKE, J. V., 338
COOKE, R. A., 644
COOMBS, R. R. A., 478
COONEY, M., 364*
COOPER, A. M., 394, 395
COOPER, I. S., 77
COOPER, P. D., 581*
COOPER, S. R., 160
COOPER, T., 66, 382
COOPER, T. J., 600
COOPER, W. C., 442, 443, 671
COOPER, W. LeG., 248
COPELAND, J. E., 124
COPELLO, F., 660
COPEMAN, W. S. C., 198, 519*
COPPO, M., 656*
CORBIN, K. B., 530
CORCORAN, A. C., 195, 359
CORCORAN, T. E., 600
CORDAY, E., 378, 379
CORDERO, A. A., 441
CORDIER, P. A., 118
CORIELL, L. L., 424
CORKILL, N. L., 488
CORNBLEET, T., 189
CORONEL, L., 47*
CORPER, H. J., 215
CORTELL, R. E., 508*
CORTI, A., 224*
COSBY, R. S., 266
COSGROVE, R. R., 125
COSIN, L., 31
COSTA, G., 503
COSTA, O. G., 512
COTES, P. M., 249*
COUCH, O. A., 210
COUMEL, H., 160
COURNAND, A., 158, 173, 458
COURT, D., 449
COURT BROWN, W. M., 589
COURTY, L., 287*
COURVILLE, C. B., 111, 409
COURVILLE, C. J., 302
COUSIN, R., 177
COUTER, W. T., 343, 344
COUVELAIRE, R., 358
COVELL, G., 442, 558
COWAN, I. C., 252
COWEN, E. D. H., 304
COX, H. R., 97
COX, L. B., 89
COXSEY, L., 169
CRAIG, G. E., 512*
CRAIG, J. M., 419*, 619*
CRAIG, R. M., 302
CRAIN, E. L., 633*
CRASKE, N., 655
CRASS, G., 25
CREAGHAN, M. V., 489
CRESSY, N. L., 562, 603
CREWE, W., 600*
CRIEP, L. H., 49, 620*
CRITCHLEY, M., 310
CROCKER, A. C., 631
CROFTON, J., 214
CRONHEIM, G., 352
CRONVICH, J. A., 234*
CROSBY, N. D., 339
CROSLEY, A. P., 574
CROSNIER, R., 106, 107*
CROSS, K. R., 600
CROTTI, G., 23
CRUICKSHANK, C. N. D., 239*
CRUICKSHANK, J. C., 239, 546*, 603
CRUISE, A. B., 420
CRUMPTON, C. W., 160, 574
CUATRECASAS, J., 406
CULBERTSON, J. W., 54, 59, 493
CULINER, A., 118
CULLUMBINE, H., 567
CULPEPPER, W. L., 381
CULVER, G. J., 245
CUMMING, H. A., 512*
CUMMINGS, M. M., 330*
CUMMINS, A. J., 574
CUNEO, H. M., 199
CUNLIFFE, A. C., 362
CUNNINGHAM, R. W., 125
CURNEN, E. C., 539
CURTI, P. C., 551*
CURTIN, M., 661
CURTIS, A. C., 193*, 292, 645
CURTIS, C. E., 300
CURTIS, J. B., 469
CURTIS, L., 137
CURTISS, C., 290
CUTBUSH, M., 135

DABIS, L., 625
DACIE, J. V., 276, 628
DACK, S., 374
DADDI, G., 105*, 552
DAENINCK, L., 14
DAHLBERG, G., 85
DAHLIN, D. C., 196
DAHLSTRÖM, G., 328
DAIMER, J., 563
DALAND, G. A., 164
DALE, H., 336*
DALEY, R., 55
DALSGAARD-NIELSEN, T., 307, 530
DALTON, A. J., 37*
DALTON, H. W., 275
DALY, R. A., 544
DAMESHEK, W., 167, 387
DAMIENS, G., 663
DAMMANN, J. F., 58
DAMODARAN, K., 181
DANARAJ, T. J., 487
DANCOFF, S. M., 138
DANIELS, J. B., 477
DANIELS, M., 547
DANIELS, T. C., 643
DANNENBURG, W. N., 352
DAŃOWSKI, T. S., 53, 144*
DARBY, W. J., 64*, 626
DARNIS, F., 396
DAS, A., 322*
DAUBER, D., 163
DAUGHADAY, W. H., 164
DAUGHERTY, N. S., 125
DAUIS-LAWAS, D. F., 496*
DAUM, S., 528
DAUPHIN, —, 537*
DAUTREBANDE, L., 341
DAVID, M., 203
DAVIDS B., 595
DAVIDSON, C. S., 230, 394, 395
DAVIDSON, H. A., 647
DAVIDSON, L. S. P., 40*, 407
DAVIES, C. E., 55, 491
DAVIES, D., 51
DAVIES, D. L., 11, 208
DAVIES, G. R., 205
DAVIS, D. J., 331
DAVIS, J. H., 274
DAVIS, J. O., 343, 617
DAVIS, L. J., 171
DAVIS, R. H., 550
DAVIS, S. K., 168
DAVISON, S., 347
DAWSON, I. M., 581*
DAWSON, J. E., 405
DAWSON, W. R., 335
DAY, E., 423*
DAY, M. J., 355
DEAN, B. H., 115
DEAN, G., 90
DEAN, R. F. A., 231
DE BEER, E. J., 233*, 458
DEBONO, J. E., 439
DEBRAY, J. R., 646
DEBRÉ, R., 149, 423, 479
DECARIS, D., 130
DECKER, J. W., 567
DECKER, K., 470
DECOURSEY, E., 468
DECROIX, E., 389, 551
DEGARA, P. F., 95
DEGENHARDT, D. P., 386
DEGOY, A. P. H., 590
DELAFONTAINE, P., 663
DELANEY, J. R., 295
DELARUE, N. C., 68
DELAUDE, A., 126
DELAY, J., 317, 535
DELCOURT, R., 104*
DE LEEUW, N. K. M., 83, 404
DELEON, J. F., 260
DELLA CASA, R., 591
DELLA SANTA, R., 354, 521
DELLE SEDIE, P. F., 330*
DELORME, E., 404*
DELWAULLE, P., 554
DE MAEYER, E., 522
DEMOLE, M., 392
DEMPSEY, A. J., 560*
DENARDI, J. M., 340
DENBER, H. C. B., 37
DENHOFF, E., 483
DENKEWALTER, R. G., 22*
DENLINGER, R. B., 472
DENNIS, E. W., 331, 440
DENNY-BROWN, D., 92, 408
DE NÓ, R. L., 13
DENT, C. E., 171
DENT, J. E., 25
DENTON, C., 485
DENTON, J. E., 571
DENZ, F. A., 464
DE PEYSTER, F. A., 304
DEPRES, H. E., 390
DERIAN, P. S., 583
DEROBERT, L., 24, 168
DE ROBERTIS, E., 603*
DE RODANICHE, E. C., 98*
DEROT, M., 84
DEROW, H. A., 247*
DERRICK, E. H., 321*
DERZAVIS, J. L., 297
DES AUTELS, E. J., 665*
DESCLAUX, P., 535
DESMARAIS, M. H. L., 405
DESTAING, F., 191, 349, 542
DESTOMBES, P., 423*
DESTOUCHES, P., 130
DE TAKATS, G., 270
DETERLING, R., 233*
DETHIER, F. M., 305*
DEUTSCH, E., 460*
DEVADAS, N. P., 552
DEVI, P., 52*
DE VRIES, A., 142, 642
DE WATTEVILLE, H., 291*
DEWHURST, K., 62
DEY, F. L., 130, 491
DHERS, V., 117
DIAMOND, I., 502
DIAMOND, J. H., 318
DIAMOND, L. K., 497
DIAS, M. V., 230*
DIBDEN, W. A., 315
DICK, G. W. A., 658
DIEFENBACH, W. C. L., 191
DIENST, R. B., 191*, 193, 513
DIETZ, M. W., 140
DIFS, H., 328
DILLARD, G. H. L., 475*
DILMAN, V. M., 270
DINGLE, J. H., 562, 603
DINIA, C., 74*
DI RIENZO, S., 172
DISCHEREIT, J., 528*
DISKANT, S. G., 232
DISTELHEIM, I. H., 390
DJIAN, A., 245
DMOCHOWSKI, L., 35
DOANE, J. C., 197*
DOBIN, N. B., 201*
DOBSON, J., 560*
DOCK, W., 265

Dodson, L. F., 621
Doherty, M. E., 11
Doig, R. K., 143*
Dole, V. P., 602
Dolger, H., 53
Dolgin, N., 267
Dolkart, R. E., 130
Doll, F., 118
Doll, R., 503
Domagk, G., 429*
Dominguez, R., 116
Domon, C. M., 578
Donald, K. W., 629
Donnet, —., 167
Donovick, R., 43
Donzelot, E., 160*, 446
Dooneief, A. S., 330*
Doret, M., 380
Dornberger, G. R., 71, 72, 283
Doshay, L. J., 414
Dotter, C. T., 266, 357, 472
Dotti, L. B., 143*, 176
Doubleday, F. N., 560*
Dougherty, W. J., 300
Douglas, J. M., 247
Dowell, A. M., 548
Dowling, H. F., 85, 239,* 420
Downs, C. M., 424
Doxiadis, S. A., 537
Dragsted, I., 330*
Dragstedt, L. R., 287
Drake, T. G., 582
Dreiling, D. A., 72
Drekter, I. J., 613
Drew, A. J., 560*
Dreyer, J. van R., 393
Droese, W., 7
Drutel, P., 457
Dryden, L. P., 568*
Duane, R. T., 628
DuBois, K. P., 354*
Dubois, R., 104*
Dubrow, H., 291
DuBuy, H. G., 229
Duca, C. J., 215
Dudgeon, J. A., 476*
Dudkina, V. K., 478
Duensing, F., 199
Duff, R. S., 91
Duffy, B. J., 588
Duffy, M., 520
Dufrenoy, J., 42
DuGraff, A. C., 233
Duguid, H. L. D., 273
Duguid, J. B., 474
Dumazer, —., 495
Dumbell, K. R., 67
Dummer, F. H. M., 479
Duncan, C. H., 533
Dunham, K. C., 228
Dunham, W. F., 87*
Dunlop, E. M. C., 82
Dunlop, R., 3
Dunn, H. J., 345*
Dunn, W. J., 249*
Dunner, L., 453, 566
Dunsford, I., 343*
Dunstan, C., 452
du Pan, R. M., 423
Duperrat, B., 219*
Durant, T. M., 232
Duthie, D. A., 299
Duthie, J. J. R., 85*, 407, 648
Dutra, F. R., 27, 465*
Dutta, S. K., 462*
Duval, A. M., 534
Duvall, R. C., 514
Duvoir, M., 24
Dwork, K. G., 333

Eads, R. B., 331
Eagle, H., 193, 235, 362
Earle, D. M., 378
Early, D. F., 9*
Early, F., 230
East, E. N., 167
East, N., 467*
Eastlake, C., 328*
Eaton, M. D., 657
Ebert, M. H., 538
Ebert, R. V., 263
Ebin, J., 202
Eckenhoff, J. E., 157
Eckerling, B., 362
Eckes, K. H., 644
Eckhardt, R. D., 230, 394, 395
Edelman, Z. I., 616*
Eder, H. A., 495
Edeson, J. F. B., 669
Edlinger, E., 422
Edmonson, H. A., 633
Edmunds, M. E., 367
Edmunds, V., 399
Edsall, G., 605
Edström, G., 522, 649
Edwards, E. A., 623
Edwards, J. E., 247
Ehrlich, R., 633* -
Ehrstrom, M. C., 485
Eiber, H. B., 56
Eichenwald, H., 220
Eisele, C. W., 663
Eisenberg, F. F., 578
Eisenberg, H., 301
Eisenberg, R. B., 597
Eisenbud, M., 452
Eisenmenger, W. J., 504
Ejrup, B., 379
Ekblad, M., 26
Ekvall, S., 650
Elam, J. O., 567*
Elam, W. N., 567*
El Borolossy, A. W., 349
Eldridge, D., 18
Elerding, A. C., 529
Elias, K., 598
Eliot, J. W., 182
Eliozishvili, K. M., 296
Elithorn, A., 351
Elkeles, A., 31
Elkinton, J. R., 403, 641
Eller, J. J., 81
Eller, W. D., 81
Ellermann, M., 312
Ellinger, G. F., 594*
Ellinger, P., 119*
Elliott, W., 3
Elliott, J., 672*
Elliott, J. A., 298*
Ellis, F., 356
Ellis, H., 349
Elmendorf, DuM. F., 191, 303
Elmendorf, E. T., 22*
Elova, M. Y., 173
Elsdon-Dew, R., 106
Elson, L., 22
Elvidge, A. R., 609
Emery, E. W., 397
Emery, J. L., 20, 127
Emmart, E. W., 43
Emmons, C. W., 144
Engel, C. E., 448*
Engel, F. L., 51
Engeset, A., 588
English, O. S., 510*
Engstrom, W. W., 582
Ensor, C. R., 650*
Entin, S., 667
Eppes, W., 324
Epstein, F. H., 619
Epstein, N. B., 655
Epstein, N. N., 400
Epstein, S., 187
Erbes, J., 585
Ereux, L. P., 512*
Erf, L. A., 167*
Erhart, E. A., 569
Eriksen, K. R., 144
Erimberger, —., 537*
Erwin, J. H., 280
Escalle, J. E., 160*
Eskola, O., 169
Espersen, E., 43
Espinoza, J., 47*
Esser, C., 139, 282
Esseveld, H., 98
Estable, J. J., 14
Eszenyi-Halasy, M., 200
Etévé, J., 167
Euler, H. E., 470
Evans, A. C., 450*
Evans, A. S., 318
Evans, D. G., 115, 366
Evans, H. M., 120*
Evans, J. A., 60
Evans, J. W., 625
Evans, R. S., 628
Evans, W., 378
Evans, W. A., 255
Evelyn, K. A., 160
Eveno, J. H., 660
Everett, G. M., 122
Everett, M. R., 249
Evold, H. L. F., 568
Evrard, E., 569

Faber, H. K., 545
Fabre, J., 521
Fähndrich, W. H., 648
Fagerberg, E., 526
Fahey, J. L., 456
Fahey, M. M., 391
Fahlstrom, S., 381
Fahrni, R., 525
Faiman, F., 577
Fainer, D. C., 503*
Fairley, D. M., 198
Fairley, N. H., 558, 671*
Falcon, W. W., 394, 395
Falkenheim, M., 635
Fanconi, G., 201*
Fanger, H., 305*
Fantes, K. H., 496*
Fantl, P., 89
Farah, A., 572
Fargo, W. C., 487*
Faribault, C., 294
Farley, J. E., 606
Farman, F., 517
Farnell, F. J., 531*
Farnsworth, E. B., 33
Farquhar, J. W., 25*, 506
Farr, A. C., 18
Farrar, B. W., 372
Farrow, R. T., 224*
Fasciolo, J. C., 174, 457
Faust, J., 354*
Favata, B. V., 36*
Fave, M., 569
Favour, C. B., 235, 363
Favre, M., 14
Favre-Gilly, J. E., 343*, 601
Fawcett, M. L., 302
Fecht, K. E., 127*
Federico Dumm, J., 260*
Fegeler, F., 298
Feinberg, A. R., 233
Feinberg, S. M., 50*
Feldman, G. B., 269
Feldman, S., 272*
Feldman, W. H., 126, 668
Fell, H. B., 36*
Feller, A. E., 562, 603
Fellinger, K., 523
Felsen, J., 393
Felson, B., 140, 357
Feltham, D. V. G., 566*
Feng, S. L., 543*
Ferayorni, R. R., 69
Ferguson, J. K. W., 640
Ferguson, M. H., 250, 476*
Fernandes, B., 535
Ferrand, —., 542
Ferrari, M., 464*
Ferraro, A., 93
Ferrebee, J. W., 305*
Ferreira, M., 418*
Ferrer, M. I., 158, 458
Fessler, A., 224*
Fetter, F., 209
Fieber, M. H., 127
Field, C. E., 367
Field, E. J., 9
Field, J., 242*
Field, J. W., 330, 331*, 669
Field, L. E., 374
Fiese, M. J., 611
Figurnov, K. M., 224*
Finch, C. A., 274, 495
Findlay, G. M., 107, 557
Findley, J. W., 284
Finkelman, I., 233, 318
Finland, M., 174, 461, 537, 543, 631
Finlay, A. C., 579
Finnerty, E. F., 537
Firestone, G. M., 417
Firminger, H. I., 58
Fischbach, H., 236*
Fischel, E. E., 333, 466*
Fischer, A., 250, 305
Fischer, A. E., 132
Fischer, F., 376
Fischer, P., 156
Fischer, W., 282
Fisher, J. H., 607
Fisher, M. M., 61*
Fishman, A. P., 197
Fitch, D. R., 649
Fitzgerald, J. D. L., 151
Fitzpatrick, M., 89
Fitzpatrick, W. H., 8
Fitzwilliams, D. C. L., 336*
Flasetti, L., 330*
Flaum, G., 302
Flax, H. J., 354
Fleck, L., 363
Fleckenstein, A., 16
Fleischner, F. G., 501*
Fleisher, M. S., 253
Fleming, J., 84
Fletcher, C. M., 228
Flippin, H. F., 20, 580
Floch, H., 423*
Florey, H. W., 461, 580
Florman, A. L., 605
Floyd, W. F., 123
Fluharty, R. G., 274
Fluker, J. L., 418*
Foley, G. E., 631
di Fonzo, M., 438
Forbes, G. B., 253
Forestier, J., 85, 86
Formijne, P., 495
Forsham, P. H., 488, 518
Foster, J. V., 249
Foulds, L., 34, 35, 249
Fournier, E., 643*
Foussier, B., 382*
Fowler, A. F., 489
Fowler, N. O., 251
Fowler, W. M., 64, 251
Fowler, W. S., 630
Fox, H. J., 178
Fox, J. P., 97
Fox, L. M., 514
Fox, N., 419*
France, W. G., 62
Franceschetti, A., 366, 380
Franchel, F., 105*
Franchini, A., 184
François, J., 46
Frank, T. V., 155
Frankel, J., 237
Frankel, J. J., 261*
Franklin, K. J., 559*
Franklin, W., 261*, 485
Franks, R., 55
Frantz, —., 289
Franzini, C., 590
Fraser, R., 397
Frazer, A. C., 370, 487*
Freedberg, A. S., 74, 293
Freede, C. L., 58
Freedman, B., 389*
Freedman, E., 172
Freedman, L. R., 381
Freeman, J., 486
Freis, E. D., 60, 125, 161, 493, 573
French, D. M., 121
French, G. N., 572
French, T. M., 614
Freudenberg, R. K., 535*
Frey, R., 234
Freyberg, R. H., 86
Fridjohn, L., 68
Friedewald, W. F., 418
Friedlaender, A. S., 369
Friedlaender, S., 369
Friedman, E. D., 91
Friedman, L. J., 246
Friedman, L. L., 531*
Friedman, M., 244, 572, 599
Friedman, N. B., 247*
Friedman, S., 110
Fries, J. H., 78
Friou, G. J., 362
Frisch, A. W., 25
Frisk, R., 487
Fritschy, W., 616

FROMMEL, E., 14
FROMMEYER, W. B., 476*
FROST, E., 39
FROST, J., 265, 377
FRUMUSAN, P., 177
FRY, N. H., 445*
FRYE, J. W., 585
FUCHS, —, 6
FUCHS, H., 388
FUJIKAWA, Y. F., 556*
FULLERTON, H. W., 273, 584
FULTON, J. F., 9*
FUREY, W. W., 381
FURMAN, M. L., 350
FURMAN, R. H., 157
FURTH, J., 95, 249*
FUST, B., 603
FUTCHER, P. H., 160, 184
FYALA, M. A., 422

GAARENSTROOM, J. H., 119
GABALDON, A., 339
GABRIELE, A. J., 53
GABRILOVE, J. L., 505
GAENSLER, E. A., 38, 279, 499
GAFAFER, W. M., 226*
GAISFORD, W., 366
GALBRAITH, A. L., 622
GALDSTON, I., 224*
GALDSTON, M., 196
GALE, E. F., 41
GALE, R. G., 157
GALLEY, R. A. E., 338*
GALLOWAY, T. C., 420
GAMBIGLIANI ZOCCOLI, A., 590
GAMMELTOFT, S. A., 559*
GAMMON, G. D., 516
GARABEDIAN, G. A., 332
GARB, J., 512
GARCIA AUSTT, E., 124
GARCIA, E. Y., 219
GARCIA LOPEZ, G., 166, 276, 411*
GARCIN, R., 651*
GARD, S., 478
GARDEL, —, 495
GARDELLA, J. W., 305*
GARDNER, C., 153
GARDNER, F. E., 619
GARDNER, F. H., 487, 627
GARDNER, G. M., 87, 198, 579*
GARDNER, H. T., 180
GARDNER, J. F., 18*
GARDNER, W. D., 112
GARDNER, W. U., 36*
GARIN, L., 472
GARLICK, H. W., 179, 394
GARNHAM, P. C. C., 107, 558
GARNIER, P., 663
GARRIDO LESTACHE CABRERA, J., 46
GARZON, H. L., 241
GASBARRINI, A., 224*
GASTON, E., 170
GATTINI, M., 373
GATZEK, H., 573
GAUL, L. E., 510
GAULTIER, M., 24
GAUNT, R. T., 202
GAUTHIER, J., 191, 542
GAUWERKY, F., 245
GAVEY, C. J., 375
GAY, L. N., 48
GAYET-HALLION, T., 570
GAZZANO, A., 467
GEAR, J., 132
GEDDA, E., 561
GEGESI-KISS, P., 213
GEILING, E. M. K., 108
GELBMAN, F., 655
GELFAND, H. H., 259
GELFAND, M. L., 61*
GELLIS, S., 76
GENECIN, A., 250
GENEST, J., 250
GEORG, J., 40, 522
GEORGE, M., 128
GERARD, R. W., 239
GERBAUX, A., 401
GERBER, I. E., 61
GERBRANDY, J., 625
GERNEZ-RIEUX, C., 554
GERRARD, J., 481
GERSHANOVICH-PALEES, L. Y., 159
GETZ, H. R., 214
GEYER, R. P., 568
GHIO, A., 660
GHIRON, V., 74*
GIANNARDI, G., 472
GIBBONS, T. B., 620*
GIBBS, E. L., 199
GIBBS, F. A., 199, 524
GIBSON, H. J., 405
GIBSON, H. J. C., 336*
GIBSON, J. E., 672
GIBSON, J. G., 63, 274
GIBSON, P. C., 620
GIBSON, S., 58
GIESE, G. K., 639
GIL, J. R., 519
GILBERT, J. L., 574
GILBERT, N. C., 121*, 491
GILCHRIST, A. R., 269
GILES, H. McC., 421
GILG, I., 625
GILL, D. C., 242
GILLANDERS, A. D., 499
GILL-CAREY, D., 18*
GILLE, G., 478
GILLESPIE, H. W., 32
GILLICK, F. G., 594*
GILLIGAN, T. J., 274
GILLORAN, J. L., 5
GILROY, J. C., 633
GIN, S. Y., 365
GINS, H. A., 560*
GINSBERG, H. S., 477
GINSBERG, J. E., 644
GIORDANO, G., 503*
GIRARD, A., 437
GIRARD, G., 451*
GIRARD, M., 250*
GIULIANI, G. M., 560*
GIUNTINI, L. S., 430
GLADSTONE, S. A., 250*
GLAZEBROOK, A. J., 11*
GLEICHMAN, T. K., 500*
GLENNY, A. T., 45*, 563
GLICKLICH, E. A., 296*
GLOBUS, J. H., 527
GLOBUS, J. H., 527
GLOVER, J. A., 115
GLUECK, H. I., 16
GLYNN, L. E., 333
GOADBY, H. K., 120
GOADBY, K. W., 120
GOCKE, T. M., 537, 631
GODFRIED, E. G., 625
GODFREY, L., 641
GOEBEL, W. F., 41
GÖLLNITZ, G., 527
GÖTTEL, M., 548*
GOETZ, R. H., 15, 272
GOLD, M. M. A., 611
GOLDBERG, B., 577
GOLDBERG, E., 221
GOLDBERG, L., 74, 458
GOLDBERG, L. C., 298*
GOLDBLATT, H., 180
GOLDBLATT, M. W., 6
GOLDEN, R., 388
GOLDENBERG, M., 233*
GOLDIN, A., 577, 578
GOLDMAN, D., 400
GOLDMAN, M. L., 184
GOLDRING, W., 195
GOLDSCHMID, E., 448*
GOLDSTEIN, A., 11
GOLDSTEIN, F., 134
GOLDSTEIN, P., 375*
GOLSETH, J. G., 408
GO LU, 16
GOMES, S., 535
GÓMEZ ORBANEJA, J., 23
GONZALEZ SORET, M., 239
GOODALE, W. T., 157
GOODALL, A. L., 60
GOODMAN, B., 490
GOODMAN, L. S., 10
GOODWIN, J. F., 57, 640
GOODWIN, W. E., 77*, 517
GORDON, I., 562, 603
GORDON, L. E., 568
GORDON, M., 254
GORDON, R. M., 600*
GORDON, S., 398
GORDON, W., 234*
GORE, I., 476
GORENS, S. W., 568
GOULD, L. N., 94
GOVAN, A. D. T., 63
GOW, R. C., 53
GOYER, R., 429
GRACE, A. W., 511
GRACE, E. J., 664
DE GRACIANSKY, P., 186
GRAESSLE, O. E., 103, 237
GRAF, K., 236
GRAFF, S., 596
GRAHAM, E. A., 68
GRAHAM, J. M., 224*
GRAHAM, J. R., 314
GRAIS, M. L., 190
GRANIRER, L. W., 648
GRANT, F. C., 410
GRASSET, E., 422
GRATER, W. C., 419
GRAUBARD, D. J., 519
GRAVESON, G. S., 307, 531
GRAY, S. J., 635
GRAYBIEL, A., 345
GRAYSON, C. E., 172
GREAVES, A. B., 646
GREEN, J. W., 36*
GREEN, M. A., 274
GREEN, S., 153
GREEN, W. R., 651
GREENBERG, J., 670, 671
GREENBLATT, I. J., 47, 272
GREENBLATT, M., 410
GREENBLATT, R. B., 191*, 193, 513
GREENE, E., 445*
GREENFIELD, J. G., 310, 311
GREENMAN, L., 53
GREENWALD, I., 111
GREER, W. E. R., 206*
DE GREGORIO, E., 81*
GREISMAN, H., 252*
GRENIER, J., 638
GREULICH, E., 514
GRIER, R. S., 6*
GRIESBACHER, O., 61
GRIFFITH, G. C., 266
GRIFFITHS, D. L., 112*, 448*
GRIFFITHS, E., 351
GRILLI, A., 592
GRILLMAYR, W., 401
GRIMSON, K. S., 268, 347*
GRISHMAN, A., 356, 374
GROB, D., 122
GROEN, H. D., 511
GROEN, J., 625
GROEN, J. J., 454*
GROFF, R. A., 653
GROKOEST, A. W., 521
GROLLMAN, A., 83, 380
GROMBAKH, S. M., 112*
GROSBERG, S., 49
GROSS, E. G., 572
GROSS, F., 571, 620
GROSS, L., 35*
GROSS, R., 278*
GROSSMAN, M., 56
GROSSMAN, M. I., 70, 189, 503*
GROSSO, O. F., 403
GRUBBS, R. C., 576
GRUBER, C. M., 15, 124
GRUBER, C. M., Jnr., 15, 124
GRÜNIG, P., 603
GRÜSSNER, G., 468
GRUHZIT, C. C., 12
GRUNBERG, E., 18
GRUNER, J., 651*
GRZYBOWSKI, M., 188, 190
GUARESCHI, G., 467
GUDE, A. V., 193
GÜLZOW, M., 7
GUGGENHEIM, K., 165*
GUGLE, L. J., 378
GUILLAUME, J., 307
GUMBINER, S. H., 264
GUMP, W. S., 347*
GUNS, P., 430
GUNTHER, M., 255
GUREVITCH, J., 362
GUTERMAN, H. S., 52
GUTHRIE, D., 335
GUTHRIE, F., 324
GUY, L. P., 454
GYE, W. E., 247
GYLLENSWÄRD, C., 337
GYÖRGY, P., 180

HAAGENSEN, C. D., 596
HAANES, M., 193*
HAAVIK, J. E., 534
HABER, H., 297
HACKETT, W. E. R., 64
HADDOW, A. J., 96, 211
HADENGUE, A., 168
HADGRAFT, J. W., 297
HAEX, A. J. C., 600
HAFKENSCHIEL, J. H., 157, 160, 574
HAFN-MEINCKE, F., 105*
HAGEDORN, A. B., 282
HAGEMANN, G., 645
HAGER, H. F., 417
HAHN, F., 65*
HAHN, G. L., 48
HAINES, S. F., 291
HALAC, E., 241
HALD, J., 23*, 353
HALDI, J., 566
HALES, H. B., 144*
HALEY, H. B., 640
HALKERSTON, J. M., 396
HALL, A. D., 195
HALL, B. E., 412, 496
HALL, D. A., 476*
HALL, G. V., 235
HALL, J. W., 476
HALL, P. W., 36
HALL, W. H., 662
HALNAN, K. E., 559*
HALPERIN, M. H., 54, 59, 493
HALPERN, B., 130
HALPERN, B. N., 16*, 458*, 517
HALPERN, L., 208
HALPERT, B., 58
HAM, D. L., 209
HAMBURGER, C., 77, 522
HAMBURGER, M., 357
HAMILTON, C. F., 291
HAMILTON, H. B., 135
HAMILTON, J. G., 28
HAMILTON, K. A., 198
HAMILTON, T. S., 568
HAMILTON-PATERSON, J. L., 319
HAMMOND, J., 9*
HAMMOND, J. B., 465
HAMMOND, M. M., 157
HAND, E. A., 300
HANDELSMAN, J. C., 157
HANICKI, Z., 65
HANNAY, P. W., 299
HANSEN, F., 23*
HANSEN, S. S., 440
HANSON, A. O., 138
HANSON, H. H., 265
HAO LI, C., 120*
HAOUR, P., 293
HARDISTY, N. M., 266
HARDT, A., 16*
HARDY, R., 566
HARGRAVES, M. M., 273
HARINGTON, A. L., 132
HARKNESS, J., 252, 405
HARLEY, D. H., 516
HARMAN, J. W., 527, 613
HARMEL, M. H., 160
HARMSEN, H., 350
HARNED, B. K., 125
HARPER, H. A., 639
HARPER, J. O., 671*
HARPOTH, H., 100
HARRELL, G. T., 97, 540
HARRINGTON, P. R., 319*
HARRIS, A., 645
HARRIS, D. A., 237*
HARRIS, J. W., 627
HARRIS, R. S., 583
HARRIS, T. N., 110
HARRIS, W., 244
HARRIS, W. B., 452
HARRIS, W. W., 401
HARRISON, C. V., 6, 266
HART, F. D., 612, 641
HART, M. V. D., 64
HART, P. L. DEV., 275

HARTMAN, A. M., 568*
HARTMANN, J., 328
HARTROFT, W. S., 595
HARTZ, P. H., 150
HARVEY, A. M., 122
HARVEY, C. C., 365, 612
HARVEY, J. C., 238
HARVEY, R. M., 158, 458
HASCHE-KLÜNDER, R., 436
HASSIN, G. B., 672*
HASSLER, R., 569*
HASTINGS-JAMES, R., 51
HATFIELD, W. H., 500
HATOFF, A., 235
HAUGAARD, N., 261, 373
HAUSER, E., 411*
HAUSS, W. H., 542, 549*
HAUVILLER, O., 151, 369
HÄVERMARK, N. G., 648
HAWARD, F. C., 312
HAWES, L. E., 590
HAWKING, F., 333
HAWKINSON, V., 39, 152
HAWLEY, C., 140
HAWLEY, J. G., 119
HAWORTH, J. B., 591
HAYES, D. W., 268
HAYMAKER, W., 22
HAYNE, R. A., 199, 524
HAYS, E. E., 627*
HEACOCK, C. H., 581
HEADLEY, N. E., 407
HEADY, J. A., 338, 351
HEAF, F., 449
HEALEY, M. M., 410
HEARD, D. H., 276
HEATLEY, N. G., 579*
HEBB, C. O., 121
HECHT, H., 190
HECHT, H. H., 491
HEEPE, F., 437
HEGSTED, D. M., 289
HEILMEYER, L., 102
HEIMANN, F. A., 562
HEIMANN, H., 226*
HEIMOFF, L., 472
HEINBECKER, P., 508*
HEINLE, R. W., 277, 608
HEINRICH, K., 159
HEISCH, R. B., 671*
HELD, R., 130
HELIKSON, J., 487*
HELLBAUM, A., 520
HELLEBERG, G., 667
HELLEBRANDT, F. A., 638*
HELLER, G., 520
HELLER, H., 177, 448*
HELLER, R., 427
HELWEG-LARSEN, P., 370
HEMPELMANN, L. H., 242
HEMPHILL, R. E., 396
HENCH, P. S., 110
HENCH, R. N., 264
HENDERSON, A. R., 215
HENDERSON, E., 213, 643
HENDERSON, F. G., 125
HENDRICKS, A. B., 71
HENDRICKS, F. D., 516
HENDRIX, J. P., 268
HENGSTMANN, H., 632
HENNEBERG, G., 253*
HENNEMAN, E., 575, 576
HENRY, J., 387
HENSCHEL, A., 611
HENSCHKE, H., 321
HENSTELL, H. H., 624
HENSTELL, I. S., 624
HERBERG, H. J., 310
HERBERT, P., 642
HERMAN, E., 88
HERMANN, K., 530
HERNADI, A., 484*
HERNANDEZ, R., 179
HERNÁNDEZ FERNANDEZ, S., 321
HERNANDEZ-MORALES, F., 486
HERRAIZ BALLESTERO, L., 151, 369
HERRELL, W. E., 19
HERRERA, G., 543
HERRICK, J. F., 585
HERRING, D. A., 346
HERRMANN, F. J., 190, 298
HERSH, A. H., 371, 405
HERSHFIELD, B. M., 334
HERSPERGER, W. G., 73
HERTIG, M., 337
HERTZ, H., 310, 650
HERTZ, M., 134
HERTZ, S., 74
HERVOUET, D., 537*
HERXHEIMER, H., 259, 369, 631
HERZ, E., 314
HERZOG, F., 423
HERZOG, W., 599
HESS, J. R., 639
HETENYI, G., 16
HEUSCHER, J., 416
HEWITT, R., 222
HEYMANS, C., 14, 15
HEYROTH, F. F., 240
HICKAM, J. B., 163
HICKMAN, E. M., 606
HIERTONN, T., 176
HIGHTOWER, J. A., 324
HILDEN, T., 195
HILKER, A. W., 267
HILL, E. L., 25
HILL, F. S., 21
HILL, J. E., 500
HILL, J. M., 25
HILL, K. R., 93
HILL, L. F., 149
HILL, L. M., 513
HILL, S. R., 518
HILL, R., 588
HILLARP, N. A., 77, 185
HILLER, F., 318
HILLIARD, J., 475
HILLMAN, R. W., 69
HILLS, A. G., 261, 373
HILLS, G. M., 579*
HILLS, O. W., 612
HINDE, I. T., 276
HINE, C. H., 125
HINSHAW, H. C., 664, 668
HINTZELMANN, U., 306*
HIRANO, N., 669*
HIRATZKA, T., 56, 492*
HIRCH, A., 561
HIRSCH, A., 236
HIRSCH, E. F., 230*, 599, 656
HIRSCHMANN, J., 267, 308, 414
HIRSH, H. L., 85
HIRSH, J., 224*
HIRSZFELD, L., 44
HITCHCOCK, F. A., 576
HITSCHLER, W. J., 210
HOBBY, G. L., 579
HOBSON, Q. J. G., 397
HOCH, H., 361*
HOCH-LIGETI, C., 248
HOECKER, F. E., 137
HOEFER, P. F. A., 314
HÖGSTEDT, C., 147
HOEKENGA, M. T., 192
HOEN, T. I., 77
HOERR, S. O., 602
HOFER, J. W., 446
HOFF, E. C., 9
HOFF, H. E., 285
HOFFBAUER, F. W., 360
HOFFMAN, S. H., 216
HOFMAN, M., 5*
HOFMANN, P., 620*
HOFFMEYER, H., 370
HOFMEISTER, M., 206
HOGGARTH, E., 437*
HOGNESS, J. R., 242
HOHENNER, K., 102, 423*
HOHENSEE, F., 346
HOLBROOK, W. A., 323, 324
HOLBURN, R. R., 134
HOLČÍK, L. J., 81
HOLDEN, R. H., 483
HOLDEN, W. D., 274, 277, 459
HOLE, N. H., 478
HOLGATE, J. A., 296
HOLLANDER, F., 72
HOLLANDER, J. L., 466
HOLMAN, R. A., 296
HOLMES, M. C., 334
HOLT, J. F., 246
HOLT, L. E., 454
HOLTON, P., 124
HOLZEL, A., 256
HOOBLER, S. W., 154, 268
HOOK, E. W., 418
HOPKINS, L. A., 255
HOPKINS, W. A., 594*
HOPPE, J. O., 12, 126, 463
HORAN, T. N., 164
HOREAU, J., 618
HORLICK, L., 163
HORMANN, H., 107
HORN, H., 374
HORNBERGER, W., 510
HORNE, G. O., 295
HORNE, N. W., 437
HORNE, S. F., 303
HORNER, J. L., 306
HORSFALL, F. L., 477
HORSTEN, G. P. M., 75
HORTLING, H., 643
HORTON, B. T., 268, 572
HORTON, C., 631*
HORVATH, S. M., 354, 466
HORWITT, M. K., 612
HORWITZ, M., 87
HORWITZ, S. A., 196
HØST, H. F., 336*
HOUGHTON, B. C., 576
HOUGHTON, L. E., 669
HOUGS-OLSEN, W., 10
HOUSTON, J., 252
HOUTZ, S. J., 638*
HOWARD, F. A., 499
HOWARD, J. E., 51
HOWARD, P. J., 47
HOWARD, W. L., 104, 665
HOWES, E. L., 643
HOWITT, B. F., 658
HOWLETT, K. S., 104
HØYER, A., 143
HOYNE, A. L., 318
HØYRUP, E., 489
HUBERT, W., 470
HUBINONT, P. O., 466*
HUBLÉ, J., 119
HUDDLESTON, O. L., 408
HUDDLESTUN, B., 372
HUFF, S. E., 511
HUGGINS, R. A., 378
HUGHES, H. O., 61
HUGHES, J. W., 560*
HUGHES, W., 54
HULBERT, B., 597
HULST, L. A., 633
HUMPHREYS, E. M., 287
HUNT, A. D., 641
HUNT, J. N., 476*
HUNT, M. L., 384
HUNTER, F. T., 137
HUNTER, G. W., 445*
HUNTER, O. B., 624
HUNTER, W. C., 68
HUPPERT, M., 79
HURLBUT, W. B., 644
HURLY, J. T., 283
HURME, V. O., 176
HURNI, H., 17*
HURST, E. W., 95, 418
HURWITZ, M. M., 186
HUSS, C. B., 136
HUSSEIN, M. K., 112*
HUSZÁK, I., 90
HUTCHINGS, L. M., 450*
HUTCHISON, D., 19, 329
HUTCHISON, J. H., 427
HUTTON, J. H., 381
HYDE, B., 109, 458
HYDE, L., 109, 458*
HYGE, T. V., 114
HYMAN, A., 197
HYMAN, G. A., 216
HYSLOP, G. H., 467

IBBOTT, F. A., 351
IKLÉ, A., 426
ILKA, S. J., 143*
ILLINGWORTH, R. S., 365
IMBER, I., 158*
IMBODEN, C. A., 671
ING, H. R., 124
INGALLS, T. H., 229
INGELFINGER, F. J., 284
INGLEMAN-SUNDBERG, A., 119
INGRAO, F., 461
INNES, E. M., 169
INNES, J., 169
IOANNOU, J., 594*
IRWIN, D. A., 341
ISAACS, J. H., 233
ISAACSON, N. H., 476
ISBELL, H., 584*
ISHIBASHI, K., 382*
ISHMAEL, W. K., 520
ISICHENKO, N. A., 249
ISRAËLS, M. C. G., 383
ISSEKUTZ, B., 16
ITANO, H. A., 496
IUNES, M., 621
IVY, A. C., 70, 393*, 570

JABLONSKA, S., 190
JACKETS, V., 25
JACKSON, A. S., 640
JACKSON, E. B., 420
JACKSON, E. L., 328
JACKSON, I. J., 609
JACKSON, M., 90
JACKSON, W. P. U., 508*
JACOB, A., 254*
JACOB, J., 352
JACOBS, M. D., 505
JACOBSEN, E., 23*, 353
JACOBSON, A. S., 520
JACOBSON, B. M., 486*
JACOBSON, G., 472
JACOBSON, L. O., 152, 170, 385, 587*
JACOBSON, S. D., 164
JACOBY, A., 646
JACQUEL, G., 208
JACQUEL, M., 208
JACQUELINE, F., 86
JACQUET, P., 168
JAEGER, R., 653
JAENIKE, J. R., 506
JAFFE, H., 293, 507
JAILER, J. W., 183
JAMES, A. H., 286, 501
JAMES, G. W., 626
JAMES, T. G. I., 653
JAMESON, J. E., 133*
JAMMET, J., 118
JANBON, M., 429, 543
JANOWITZ, H. D., 189, 503*
JANUS, W. L., 140
JAQUES, L. B., 134
JAQUETI DEL POZO, G., 29
JARIA, A., 654
JAROS, S. H., 233*
JASINSKI, B., 612, 627
JASPER, H., 524
JAUERNIG, R., 246
JAWETZ, E., 132
JAWORSKI, A. A., 540, 606
JEAN, R., 551*
JEFFERSON, G., 560*
JEFFERY, G. M., 671
JEND, W., 485
JENKS, A. L., 168
JENNINGS, A. F., 594
JENNINGS, G. H., 319
JENNINGS, M. A., 461
JENSEN, H., 8
JERSILD, T., 530
JERVIS, G. A., 484*
JEWESBURY, E. C. O., 411
JILLSON, O. F., 79
JIMÉNEZ DÍAZ, C., 144
JOANNOU, J., 326
JOEKES, A. M., 304
JOHN, H. J., 489
JOHNS, L. E., 260
JOHNSON, B. A., 188
JOHNSON, J. E., 577*
JOHNSON, K. D., 619
JOHNSON, S. A. M., 303*
JOHNSON, T., 398
JOHNSTON, J. A., 47
JOHNSTONE, D. F., 418*
JOHNSTONE, H. G., 440
JOHNWICK, E. B., 292*
JOKIPII, S. G., 197*
JOLLES, B., 355
JOLLIFFE, N., 1
JOLLY, P. N., 556*
JONES, A. R., 336*
JONES, D., 564
JONES, D. P., 469
JONES, E., 64*

JONES, E. M., 665
JONES, F., 25
JONES, F. A., 503
JONES, G., 126
JONES, L. C., 560*
JONES, M. F., 439
JONES, O. R., 665
JONES, P. F., 351
JONES, R. O., 655
DE JONGH, D. K., 125
DE JONGH, S. E., 119
JONGKEES, L. B. W., 454*
JÖNSSON, B., 525
JOPLING, W. H., 4
JOPPICH, G., 419
JORDA, M., 408
JORDAN, C. F., 450*
JORDAN, R. G., 21
JORDAN, W. S., 565
JOSEPH, H. L., 297
JOSEPHY, H., 309
JOULES, F. E., 218
JOWETT, A. E., 141
JUBELIRER, R. A., 16
JUDD, A. R., 215
JÜNEMANN, P., 550
JUNG, P., 559*
JUNGE, H., 31
JUNGE, J. M., 328
JUNGMANN, H. J., 31
JUNKERSDORF, J., 648

KAAE, S., 77
KABAT, E. A., 567
KABELITZ, H. J., 495
KABLER, P., 364*
KAHLER, H., 37*
KAHN, M. C., 444
KAHN, R. L., 45*
KAINDL, F., 59, 412
KAISCH, A. M., 634
KALBFLEISCH, H. H., 555
KALDEGG, A., 198, 654*
KALIL, T. H., 140
KALK, H., 638
KALTER, S. S., 320*
KAMENETSKAYA, R. A., 2
KANE, G. G., 119*
KANE, J. H., 579
KANNER, L., 207
KANTER, L., 17*
KAPFERER, J. M., 553
KAPLAN, A., 575
KAPLAN, H., 36*
KAPLAN, L. I., 410
KAPLAN, S. R., 132, 236, 264
KARAILA, E., 330*
KARAMCHANDANI, P. V., 552
KARATCHENTZEFF, N., 130
KARCH, H., 553
KARISTRÖM, F., 482
KARLSON, A. G., 126
KARP, D., 285
KARPINSKI, F. E., 608
KARTUS, S., 166
KASS, E. H., 537
KATTUS, A., 250
KATUGAMPOLA, D. C., 364
KATZ, A., 15
KATZ, E., 329
KATZ, L. N., 56, 163, 264, 267, 378
KAUFFMAN, J., 602
KAUFMAN, I. C., 206*
KAUFMANN, A., 554
KAUFMANN, H., 160*, 446
KAUFMANN, L., 40*
KAUMP, D. H., 606
KAUTZKY, R., 309*
KAVKA, J., 447
KAYE, S. L., 162
KEATING, F. R., 291
KEATING, R. P., 36, 154
KEELE, K. D., 178
KEEPE, W. G., 462*
KEESER, E., 75
KEEVIL, J. J., 336*, 448, 560
KEHRER, H. E., 526
KEIL, H., 447
KEITH, M. A., 269
KEIZER, D. P. R., 583
KELEMEN, E., 170
KELLEHER, W. H., 319
KELLER, A. D., 454
KELLER, M. J., 322
KELLNER, B., 639
KELLY, D. R., 18
KELLY, H. G., 618
KELLY, K. H., 249
KELLY, M. G., 37*
KELSALL, A. R., 231
KELSEY, F. E., 108
KEMP, S., 503
KEMPNER, W., 494
KENAWY, M. R., 56
KENDALL, D., 309
KENDALL, E. C., 110
KENDALL, F. E., 163
KENIGSBERG, S., 76
KENNARD, M. A., 88
KENNAWAY, E. L., 338
KENNEDY, A. F., 405
KENNEDY, J., 339
KENNEY, M., 222
KENNEY, R. A., 120
KERCKHOFF, K., 377
KERLEY, T. G., 138
KERSHMAN, J., 205
KERST, D. W., 138
KERT, M. J., 154
KETRON, K. C., 454
KETY, S. S., 157, 160, 267
KEY, J. M., 400
KEYES, J. W., 154
KEYS, A., 511, 611
KHALIL, A., 661
KHAZANOV, A. T., 474
KHROMOV, B. M., 224*, 559
KIDD, P., 64
KIDIYOOR, S. R., 552
KIELER, J., 370
KIELHOLZ, P., 94, 416
KIERLAND, R. R., 19, 296*
KILBOURNE, P. C., 578
KILHAM, L., 418
KIMMELSTIEL, P., 298*
KING, E. J., 6, 567*, 600
KING, E. Q., 578
KINGSLEY, J. W., 641
KINSELL, L. W., 39, 639, 643
KINSELLA, V. J., 141
KIRK, E., 161*
KIRKLIN, B. R., 158
KIRKPATRICK, N. R., 52
KIRMSE, T. W., 217
KIRSCHON, A., 587*
KIRSNER, J. B., 71, 284, 287, 289, 636
KISSLING, R. E., 43
KISTIN, A. D., 55
KITCHEN, D. K., 516
KITCHEN, S. F., 211
KITZMILLER, K. V., 240, 465*, 584*
KJELLBERG, S. R., 455
KLATSKIN, G., 394
KLAUDER, J. V., 188
KLAUE, R., 526*
KLEIN, D., 366
KLEIN, H. A., 56, 492*
KLEIN, R., 9*
KLEINSORG, H., 75
KLIGMAN, A. M., 297*
KLINE, B. S., 497, 596
KLOPSTOCK, R., 434
KNAUB, V., 567
KNOEVENAGEL, C., 234
KNOPPERS, A. T., 125
KNORR, R., 549
KNOTT, J., 199
KNOWLTON, A. I., 183
KNOWLTON, M., 180
KNOWLTON, N. P., 242
KNOX, J. A. C., 57
KOBERNICK, S. D., 36*, 388
KOCH, D. A., 215
KOCH, E., 165*
KOCH, F., 549
KOCH, J., 574
KOCH, K. W., 138
KOCSÁN, C., 130
KOEGLER, S. J., 481
KOEHN, C. J., 8
KOENIG, E. C., 245
KOEPCHEN, A., 666
KOERNER, T. A., 214
KOETS, P., 397
KOHÁRI-KUCHÁRIK, J., 622
KOHLER, C. E., 135
KOHLER, L. M., 245
KOHN, J. L., 132, 236, 527
KOHN, K. H., 657
KOLACHEV, A. A., 259
KOLMER, J. A., 645
KOLODNY, M. H., 520
KONZETT, H., 121, 575
KOPECNY, L., 200*
KOPP, I., 192
KOREF, O., 261
KORPÁSSY, B., 170
KOSOVSKIIN, Y. Y., 259
KOSTKOWSKI, A., 65
KOSZALKA, M. F., 639
KOSZEWSKI, B. J., 37
KOTEEN, H., 192
KOTHARI, B. V., 626
KOTTER, G. F., 209
KOUNTZ, W. B., 161*
KOURILSKY, R., 389, 643*
KOURILSKY, S., 389, 551
KOUWENAAR, W., 98
KOVÁCS, Á., 592
KOVACS, Z., 511
KOVAR, E., 263
KOVAR, E. B., 4*
KOWAL, S. F., 424
KOWALCZYKOWA, J., 16
KOWALEWSKI, K., 313, 346
KOZLOV, L. A., 453
KRAATZ, C. P., 15, 124
KRAKUSIN, J. S., 33
KRAMER, B., 508*
KRAMER, P., 284
KRAVCHICK, D. I., 251
KRAYER, O., 11
KRAYO, J. C., 532
KREBS, C., 589
KREIS, B., 430, 431
KREITNER, H., 635
KREMER, V. L., 195
KRÖBER, E., 206
KROLL, F. W., 471
KROMSIGT, G. K. L., 625
KROÓ, H., 82
KROOP, I. G., 197
KRUGER, H. E., 378
KRUSE, W. T., 645
KRUSEN, F. H., 412, 585
KUBIK, M., 577
KUGELBERG, E., 9, 89
KUH, C., 235
KUHLMANN, F., 549
KUHN, J. F., 520
KUKUEV, L. A., 224*
KUNA, S., 21
KUNKEL, H. G., 504
KUO, P. T., 617
KURNICK, N. B., 127
KUSKE, F., 419
KUSKIN, L., 263
KUSSEROW, G. W., 271
KUTCH, J. H., 605
KUZELL, W. C., 87, 198
KWANTES, C. M. S., 419
KWITOWA, H., 545
KYDD, D. M., 582
KYLE, L. H., 77*

LABAN, M., 435
LABHART, A., 426, 624
LABOCCETTA, A. C., 422, 528
LACK, A., 579*
LACKEY, M. D., 229
LACKMAN, D. B., 656
LACY, H., 131
LADÁNYI, J., 342
LADELL, W. S. S., 7, 485
LADEN, E. L., 296
LADENHEIM, J. C., 672*
LAFFARGUE, —., 495
LAGERCRANTZ, R., 607
LAGERLÖF, H., 230
LAGO, H. D., 519
LAHIRI, S. C., 462*
LAIRD, R. L., 220
LAKEN, B., 394
LALICH, J. J., 596
LALLI, G., 213
LAMBERT, E. H., 345
LAMOTTE, M., 396
LAMPE, I., 215
LAMPE, P. H. J., 543*
LAMY, M., 118
LANCHY, P., 105*
LAND, F. T., 634
LANDAU, D., 192
LANDE, M., 241
LANDEN, H. C., 553, 555
LANDING, B. H., 577, 578
LANDIS, S. N., 600
LANDMESSER, W. E., 249
LANDOWNE, M., 380
LANES, A. M., 12, 126, 346, 463
LANDTMAN, B., 264, 480
LANE, C. G., 228*, 509
LANE, R. E., 226
LANG, L. P., 389
LANG, W., 417
LANGE, K., 611
LANGERON, P., 287*
LANGMUIR, A. D., 562, 603
LANGUILLE, M., 658*
LANGUILLON, J., 423*
LANKFORD, C. E., 131
LANNING M., 262
LANZL, E. F., 138
LANZL, L. H., 138
LAPI, A., 289
LARIZZA, P., 8*, 277, 306
LARKIN, M., 130
LARSEN, V., 23*, 353
LARSON, C. L., 450*, 662
LARSON, E. A., 152
LARSON, R. D., 128
LARSSON, L. G., 29
LARUELLE, L., 204
LASKOWSKI, J., 38
LASSEN, S., 345*
LAUDICELLA, V., 24
LAUG, E. P., 240
LAUGHLIN, J. S., 138
LAUGHLIN, M. E., 301
LAURIE, W., 333
LAURITZEN, E., 463
DI LAURO, S., 117
LAVARACK, J. O., 455
LAVENNE, F., 264, 452
LAWRENCE, H. S., 364
LAWRENCE, J. H., 169, 386
LAWRENCE, J. S., 361*
LAWSON, J. H., 418
LAX, F., 489
LAYMON, C. W., 368
LEAF, A., 343, 344
LEARD, S. E., 206*
LEATHAM, A., 271
LE BEAU, J., 411*
LECHEVALIER, H. A., 237*
LECOCQ, E., 21
LECOQ, R., 34*, 151, 583, 584
LEDER, M. M., 500*
LEDERER, J., 185
LEE, A. J., 88
LEE, R. E., 10
LEES, J. C., 3
LEFEBVRE, P., 106
LEFLER, J. S., 579*
LEGER, L., 241
LEGEŻYŃSKI, S., 16
LEHANE, D., 419
LEHMAN, A. J., 462
LEHMANN, G., 347
LEHMANN, J., 667
LEHNER, H., 399
LEHR, D., 17*
LEICHER, F., 67
LEIDY, G., 145
LEIFER, E., 242
LEIGH, A. D., 310
LEIGH, T. F., 594*
LEIGHTON, R. S., 471
LEIMBACH, G., 436
LEINER, G. C., 57, 430
LEITES, S. M., 248
LEITTER, H. E., 197
LEIZEROVSKAYA, E. G., 173
LELAND, L. S., 297
LEMAIRE, M., 358
LEMBERGER, A., 435
LEMLEY, J. M., 157
LEMON, B. K., 606
LENARSKY, M., 319*

LENDLE, L., 346
LENNETTE, E. H., 115, 238
LEOPOLD, —., 275
LEPINE, P., 603
LEPORSKII, N. I., 448*
LEPOW, H., 252*
LEPPER, M. H., 239*, 420
LERMAN, I. A., 224*
LERNER, E. M., 41
LERNER, H. B., 639
LESH, J., 446*
LESLIE, S. H., 394
LESNE, E., 431
LESNITSKAYA, V. L., 200
LESNÝ, I., 200
LESTER, W., 561
LETTERER, E., 37, 474
LEVADITI, C., 126, 437, 645, 660
LE VAY, D., 522
LEVENSON, S. M., 465
LEVESON, I., 352
LEVIN, B., 366
LEVIN, E., 71, 636
LEVIN, S., 410
LEVINA, S. V., 453
LEVINE, L., 605
LEVINE, M. I., 49
LEVINE, P., 118*
LEVINE, R., 52, 372
LEVINE, S. A., 377*
LEVINSON, A., 329*, 431
LEVINSON, L., 279, 486
LÉVINTON, J., 260*
LEVY, H., 47
LEVY, J. S., 71
LEVY, M., 661
LEVY, P., 437
LEVY, R. L., 616
LEW, E., 545
LEWIN, D. C., 70
LEWIN, E., 522
LEWINN, E. B., 582
LEWIS, A., 11
LEWIS, A. E., 492
LEWIS, H. D., 63
LEWIS, I. C., 25*
LEWIS, L. G., 244
LEWIS, N., 637
LEWIS, R. C., 470
LEWIS-FANING, E., 365
LEWTHWAITE, R., 320, 421
LEY, H. L., 320, 421, 660
LI, M. H., 36*
LIBBRECHT, L., 14
LIBET, B., 455
LICHNER, G., 640
LICHTENSTEIN, A., 563, 610, 633
LICHTENSTEIN, M. R., 551, 667
LIDWELL, O. M., 561
LIDZ, T., 262
LIEBERT, E., 318, 612
LIEBOW, A. A., 468
LIFSCHITZ, C., 389
LIGHTBODY, H. D., 568
LILLE-SZYSKOWICZ, I., 44
LILLIE, R. D., 538
LIMARZI, L. R., 624
LIMAURO, A. B., 96
LINCOLN, C. S., 644
LINCOLN, E. M., 217
LIND, J., 469*
LINDER, J. M., 272*
LINDERT, M. C. F., 639
LINDGREN, G., 273
LINDSAY, S., 38*
LING, C. C., 445
LINGS, H., 30
LINKE, A., 102
LINZ, R., 21, 104*
LITHANDER, A., 101
LITTER, J., 493
LITTLE, R. C., 119
LITTLE, S. C., 200, 410
LITTMAN, A., 70
LITTMANN, D., 267
LIVINGSTON, G. S., 419*
LIVINGSTON, S., 530
LIVINGSTONE, R., 102, 552
LLOPART, J., 403
LLOYD, B. J., 37*
LOBSENZ, H., 246
LOCKHART, R. J. J., 566*
LOCKIE, L. M., 86
LÖHE, H., 82
LOESER, A., 75
LOEW, E. R., 12
LOEWE, L., 56, 169
LOEWENTHAL, L. J. A., 398, 566*
LÖFGREN, O., 29
LÖFSTRÖM, G., 114
LOGAN, A., 281
LOGAN, M. A., 513
LOGE, J. P., 170
LOGG, M. H., 217
LOKEN, A. C., 22
LONG, E. R., 214
LONG, J. H., 232
LONG, P. H., 461
LONGHI, A., 295
LONGINO, F. H., 347*
LOOFBOUROW, D. G., 622
LOPEZ TOCA, R., 166, 276, 411*
LOPUSNIAK, M. S., 286
LORBER, J., 606
LORENZ, W., 244
LOTMAR, R., 586
LOTTE, A., 326, 430, 431
LOVE, L., 455
LOVELACE, F. E., 119*
LOVELOCK, J. E., 67
LOW-BEER, B. V. A., 169
LOWE, C. U., 633*
LOWE, J., 659
LOWE, K. G., 304
LOWELL, F. C., 261*, 485
LOWEN, H. J., 374*
LOWRY, H., 254
LOWRY, O. H., 1, 454
LOWYS, P., 150, 328
LOXTON, G. E., 522
LUCAS, C. C., 595
LUCCHESI, M., 105*, 552
LUCIA, S. P., 276, 384
LUCKNER, H., 153
LÜBBERS, P., 165*
LÜCHTRATH, H., 8
LÜDERS, C. J., 37*
LÜHR, K., 321
LÜSCHER, E., 624
LUETSCHER, J. A., 195
LUFT, R., 74, 76, 119
LUKASHEV, V. A., 60
ŁUKASZCZYK, F., 30
LUMSDEN, W. H. R., 96
LUNDGREN, K. D., 134
LUNN, V., 536
LUSHBAUGH, C. C., 36*, 239
LUSKY, L. M., 240
LYNCH, F. W., 398
LYNCH, J. P., 38
LYONS, R. H., 268

MA, R. A., 349
MCAFEE, G. D., 512*
MACARTHUR, P., 666
MCAVOY, M., 200
MCBRIDE, A., 167*
MCCALLIE, D. P., 639
MACCALLUM, F. O., 319
MCCALLUM, N. E. W., 26
MCCANCE, R. A., 231
MCCAWLEY, E. L., 458
MCCAY, C. M., 119*, 502
MCCLURE, G. Y., 138
MCCONNELL, A. A., 411
MCCORRISTON, J. R., 71*
MCCORT, J. J., 472
MCCRACKEN, I. E., 224*
MCCREIGHT, W. G., 297*
MCCRORY, W. W., 641
MCCULLOCH, R. P., 163
MCCULLOUGH, N. B., 663
MCCUTCHEON, M., 597
MCDERMOTT, E. B., 45*
MACDONALD, A., 146
MCDONALD, E. K., 489
MACDONALD, I. R., 391
MCDONALD, J. R., 38, 282
MCENERY, E. T., 433
MCEVEDY, M. B., 48*
MACFARLANE, W. V., 445
MCGAVACK, T. H., 76, 531*, 613
MCGRAW, R. B., 207
MACGREGOR, A. G., 122
MACGREGOR, A. R., 482
MCGREGOR, T., 331
MACH, R. S., 260, 521
MACHELLA, T. E., 288
MACHT, D. I., 20
MCINTIRE, F. T., 162
MCINTOSH, G. A., 539*
MACK, J. K., 618*
MCKAY, D. G., 38
MACKAY, M., 179
MACKAY-DICK, J., 209
MCKEE, R. W., 495
MACKENZIE, D. W., 71*
MACKERRAS, I. M., 607*
MACKINNON, J., 491
MCKUSICK, V. A., 560*
MACLAGAN, N. F., 503, 641
MCLARDY, T., 208
MCLAUGHLIN, A. I. G., 228
MCLEAN, C. R., 33
MACLEAN, H., 129, 657
MCLEAY, D. B., 539*
MACLENNAN, M. F., 45*
MACLEOD, J., 23*
MACMAHON, A., 610
MCMANUS, M. J., 293*
MCMENEMEY, W. H., 402*
MACNALTY, A. S., 560
MCQUARRIE, I., 290
MACRAE, J., 318
MCVAY, L. V., 220, 324
MADAJEWSKI, D. S., 254*
MADDEN, E. E., 381
MADDEN, J. F., 368
MADDOX, K., 182
MAGAREY, F. R., 157
MAGAZANIK, M. L., 336*
MAGENDANTZ, H., 158*
MAGNUSON, H. J., 193*, 513
MAGNUSSON, J. H., 101, 478
MAGOFFIN, R., 438
MAGOUN, H. W., 491
MAGRASSI, F., 541
MAGUN, R., 307
MAHAFFY, A. F., 211
MAHAUX, J., 313, 346
MAHONEY, J. F., 645
MAIER, C., 376
MAIER, G., 415
MAINOLI, S., 616*
MAINZER, F., 488
MAIR, C. M., 167
MAISON, G. L., 271
MAIZELS, M., 7*
MAJOR, R. H., 560*
MALAGUZZI VALERI, C., 66*
MALINER, M. M., 446
MALLUCHE, H., 437
MALMROS, H., 176, 334
MALONEY, M. A., 465
MALONEY, W. J., 335
MALTON, S. D., 268
MALUF, N. S. R., 196
MALZONE, L., 143*
MAN, E. B., 582
MANCEAUX, G. A., 408
MANDELSHTAM-VOLINSKAYA, L. M., 156
MANDERSON, W. G., 418
MANKIKAR, D. S., 402
MANN, F. D., 250
MANN, G. V., 153
MANN, I., 249*
MANQUÈNE, —., 663
MANSON-BAHR, P., 106
MANTHA, L., 407
MANTOOTH, W. B., 301
MANTOUX, G., 430
MANZANEK, H., 375
MARAL, R., 110
MARBLE, A., 53, 489
MARC-ANTOINE, H., 160
MARCEL, J. E., 551
MARCHETTI, G., 233*
MARCONI, F., 270
MARCONI, R., 503
MARCUS, R. E., 199
MARCUSSEN, R. M., 532
MARECAUX, L., 429
MAREN, T. H., 333*
MARESH, F., 104
MARGEN, S., 639
MARGOLIS, H. M., 405
MARGULES-LAVERGNE, M. P., 588*
MARILL, F. G., 5*
MARILLIER, —., 118
MARINELLI, L. D., 588
MARINELLI, P., 608
MARKEES, S., 371
MARKEL, J., 79
MARKS, D. N., 334
MARKS, E. K., 170
MARKS, I. E., 79
MARKS, J. A., 288
MARKSON, D. E., 407
MARMELZAT, W. L., 224*
MAROT, R. J., 106
MARRACK, J. R., 361*
MARSH, D. F., 346, 574
MARSH, J. B., 261, 373
MARSHALL, C., 524
MARSHALL, H. E. S., 94
MARSTON, R. Q., 580*
MÅRTESNSSON, J., 76
MARTIN, A. R., 437*
MARTIN, C. G., 393*
MARTIN, F., 282
MARTIN, J., 517
MARTIN, L., 637
MARTIN, R., 651*
MARTIN, S. P., 51
MARTIN, W. J., 451
MARTINETTO, G., 490
MARTINS, A. A., 418*
MARTYN, G., 256, 481
MARZONI, F. A., 268
MASLAND, R. L., 410
MASON, A. S., 396
MASON, L. M., 298*
MASSELL, B. F., 518
MASSHOFF, W., 37
MASSON, G. M. C., 195, 359
MASSON, J. M., 129
MAST, G., 193
MASTER, A. M., 374
MATEER, F. M., 53
MATHESON, N. M., 224*
MATHESON, W. J., 390
MATSUI, M., 669*
MATTEINI, M., 137*
MATTHES, K., 573
MATTHEWS, LER. W., 568
MATTICK, A. T. R., 236
MATVEEV, K., 253
MAUZÉ, J., 423*
MAVOR, R. H. M., 565
MAY, C. D., 633*
MAYER, W. D., 581
MAZINA, E. G., 3
MAZOUÉ, H., 151, 584
MAZZELLA, H., 15
MEADS, M., 97
MECHELKE, K., 573
MEHL, J. W., 633
MEIER, R., 571
MEIKLEJOHN, A., 341
MEIKLEJOHN, G., 145, 147, 238
MEILMAN, E., 486*
MEINERT, J. K., 360
MEININGER, W. M., 186
MEINKEN, M. A., 249*
MEITES, J., 75
MELENEY, H. E., 221
MELIN, G., 563, 565
MELLANBY, E., 112*
MELNICK, J. L., 318, 539
MENDELSON, E. S., 455
MENDLOWITZ, M., 61
MENEELY, G. R., 157
MENEGHELLO, J., 47*
MENG, H. C., 230
MENKIN, V., 595
MERCHANT, W. R., 405
MERGONI, G., 464*
MERKEL, W., 436
MERLE, —., 107*
MERRILL, O. E., 137
MERRINGTON, W. R., 204
MERRITT, H. H., 651
MERSKEY, C., 384
MERTENS, A., 669*
MERTENS, H. G., 308
MESSERSCHMITT, J., 164
METCALF, B. H., 347*
METIVIER, O., 150
METTIER, S. R., 167*
MEYER, F. W., 371
MEYER, K. A., 126*, 180

MEYER, L. M., 275
MEYER, O. O., 576
MEYER, P., 56
MEYER, P. D., 140
MEYER, R. B., 324
MEYER, S. N., 429*
MEYER-BRUNOT, H. G., 343
MEYER-MICKELEIT, R. W., 525
MEYERS, M. C., 165
MEYERS, R., 199
MICETICH, A., 12
MICHAELS, G. D., 39
MICHAIL, J., 650
MICHELAZZI, A. M., 664
MICHELSON, H. E., 80*
MICHELSON, J. P., 508*
MICHEZ, J., 518
MICHIE, A. J., 349
MICHTOM, R. J., 57
MICKEY, S., 200*
MIDANA, A., 298
MIDDLEMISS, J. H., 246
MIDDLETON, J. W., 539
MIEDZIŃSKI, F., 188
MIESCHER, G., 511
MIGAZZO, C., 131
MIGLIACCIO, A. V., 417
MIGLIARO, E., 15
MILANES, F., 166, 276, 411*
MILANI-COMPARETTI, A., 433
MILBERG, I. L., 189
MILHAM, M., 587*
MILLAR, J. H. D., 411
MILLER, C. P., 22
MILLER, F. J. W., 114
MILLER, H., 640
MILLER, J. H., 624
MILLER, J. J., 545
MILLER, J. L., 188
MILLER, J. M., 363
MILLER, M. L., 615
MILLER, O. B., 189
MILLER, P. A., 41
MILLER, R. N., 354
MILLER, T. H., 295
MILLS, G. Y., 378
MILLS, H., 276
MILLS, M. D., 158
MILLS, S. D., 382
MILLS, W. G., 258
MILNOR, J. P., 234*
MILSTONE, J. H., 568*
MILZER, A., 129, 657
MINDLIN, J., 665*
MINGLE, C. K., 450*
MINOZZI, A., 497
MINTZ, R. S., 329
MIRICK, G. S., 238, 504
MISIEWICZ, J., 216
MITCHELL, G. A. G., 559
MITCHELL, E. R., 341
MITCHELL, H. H., 568
MITCHELL, N., 47
MITCHELL, P., 235*
MITCHELL, R. S., 433, 434
MLCZOCH, F., 382
MODI, C. J., 544
MOE, G. K., 12
MOE, R. H., 397
MOEHLIG, R. C., 148
MÖLLER, E. F., 234
MOIR, W. W., 358
MOISTER, F. C., 60, 125, 493, 573
MOLANO, P. A., 121
MOLE, R. H., 295
MOLES, R., 179
MOLESWORTH, B. D., 659
MOLINIER, A., 106
MOLITOR, H., 21
MOLLE, W. E., 638
MØLLER, E., 316, 527
MÖLLER, F., 309*
MØLLER, K. O., 23*
MOLLISON, P. L., 135
MOLLWEIDE, H., 316
MOLONEY, W. C., 143*
MÓNACO, R., 422
MONT, F. G., 519
MONTÉZIN, G., 352
MONTGOMERY, A. H., 30*
MONTGOMERY, D. C., 30*
MONTGOMERY, D. M., 127
MONTGOMERY, H., 297*
MONTGOMERY, R. M., 30*
MONTO, R. W., 154
MOODY, J. P., 450
MOOLTEN, S. E., 272, 490, 623
MOONEY, A. J., 411
MOORE, A., 143*, 179
MOORE, A. E., 248
MOORE, C. V., 169
MOORE, D. H., 596
MOORE, D. J., 180
MOORE, J. R., 388
MOORE, P. E., 1
MØRCH, E., 41
MORE, R. H., 33, 36*
MORELY, G. R., 568
MORGAN, A. D., 142
MORGAN, E. A., 301
MORGAN, E. H., 496
MORGANS, M. E., 640
MORGENSTERN, P., 357
MORLAN, H. B., 25
MORLAND, A., 501
MORLOCK, C. G., 69
MORLOCK, H. V., 552
MORRIS, K. R. S., 226
MORRIS, L. C., 665*
MORRISON, L. M., 272, 619
MORRISON, M., 169
MORTON, J. H., 343*
MOSER, P., 401
MOSINGER, M., 36*
MOSONYI, L., 130
MOSS, A. H., 47
MOTE, J. R., 627*
MOTTERAM, R., 143*, 179, 394
MOUNTIN, J. W., 4*
MOUREN, P., 133
MOYER, J. H., 574
MOZZICONACCI, P., 149
MUDGE, G. H., 183
MUELLER, E. E., 104
MUELLER, J. H., 41
MÜLLER, J. H., 138
MÜLLER, R. W., 246
MUIR, A., 502
MUIRHEAD, E. E., 25, 83, 380
MUIRHEAD-THOMSON, R. C., 586
MULINOS, M. G., 186
MULLER, M. B., 618
MULLY, K., 376
MUNCH-PETERSEN, S., 530
MUNGER, R. S., 224*
MURGATROYD, F., 332
MURPHY, B. M., 396
MURPHY, G. E., 223
MURPHY, J., 250
MURPHY, J. C., 81
MURPHY, J. D., 553
MURPHY, T. L., 394
MURRAY, E. S., 98
MURRAY, G., 404*
MUSSELMAN, A. D., 362
MUSTARD, H. S., 530
MUTCH, N., 176
MUTH, H., 468
MYERS, G. B., 56, 492*
MYERS, J. A., 668
MYERS, R. J., 118*
MYHRE, J., 283
MYLON, E., 381
MYNORS, L. S., 276

NABARRO, J. D. N., 278
NACHMANSOHN, D., 12
NADLER, C. S., 262
NAGAMATSU, G., 398
NAGELSCHMIDT, G., 6
NAGFY, S. F., 572
NAGLEY, M. M., 217
NAIRN, R. C., 175
NALEFSKI, L. A., 121*
NALLS, W. L., 357
NARAYANASWAMI, P. S., 659
NARSETE, E. M., 345
NASSAU, E., 218
NASSET, E. S., 506
NATAF, R., 105*
NATHAN, P. W., 204, 256
NEAL, W., 385
NEDELJKOVIC, J., 435
NEEDHAM, G. M., 132
NEEDHAM, J. W., 373
NEEL, J. V., 382*
NEILL, C. A., 366
NEIMANN, N., 258
NEIMARK, O., 392
NELIGH, R. B., 165, 268
NELSON, C. T., 387
NELSON, J., 423
NELSON, P. A., 585
NELSON, W. E., 424
NEMOURS-AUGUSTE, S., 342
NESBITT, S., 283
NETTO, J. A., 112*
NEUBAUER, C., 95
NEUBURGER, M., 672*
NEUHAUSER, E. B. D., 473, 633*
NEUMANN, C. Z., 149
NEUMANN, M. A., 309
NEVILLE, J. F., 567*
NEWBURGH, L. H., 344
NEWCOMBER, V. D., 193*
NEWMAN, A. A., 601
NEWMAN, E., 250
NEWMAN, L. F., 559*
NEWTON, G. G. F., 579*
NEWTON, W. A., 390
NEWTON, W. I., 439
NEY, H., 587
NEYMANN, C. A., 201*
NIAZI, S., 287*
NICHOL, A. D., 116
NICHOLS, A. C., 349
NICHOLS, D. R., 132
NICHOLSON, H., 281
NICKEL, K. C., 109
NICKERSON, M., 347*
NIE, L. W., 92
NIEDERMEIER, W., 522
NIELSEN, A. L., 494
NIELSEN, H., 589
NIEMEYER, P., 138
NIERO, G., 607
NIGST, H., 224*
NOALL, M. T., 208
NOE, H. A., 577, 578
NOGUER MORE, S., 188
NOMLAND, R., 622
NOORDAM, A. L., 5*, 657
NORCROSS, B. M., 86
NORDENSON, N. G., 648
NOR EL DIN, G., 537*
NORMAN, R. M., 203
NORTHFIELD, D. W. C., 355
NORTON, D. H., 645
NOSTER, K., 350
NOTARIO, A., 277
NOTTER-BLUM, A. H., 36
NOUAILLE, J., 618
NOVAK, M., 42
NOVEL, E., 422
NUSSEY, A. M., 289

OAKES, W. R., 242
OAKLEY, C. L., 146
ÖBERG, G., 544
OBRTEL, J., 187
O'CONNOR, J. B., 104, 433
ODEBLAD, E., 77
ODEL, H. M., 403
ODIER, J., 260
ODOM, G. L., 129
O'DRISCOLL, D. T., 389
VON OETTINGEN, W. F., 464*
OFFENHAUSER, W., 444
OGILVIE, C. M., 565
OGINSKY, E. L., 603, 604
OGNEV, B. V., 619
OLANSKY, S., 516, 646
OLBRICH, O., 250*, 476*
OLDENBURG, B., 549*
OLDFELT, V., 418
OLDHAM, P. D., 228
O'LEARY, P. A., 19, 303
OLESEN, H., 475
OLITSKY, P. K., 249*
OLIVEIRA CUNHA, H., 511
OLIVEIRA MORAIS, F., 512
OLIVER, E. A., 644
OLIVER, J., 84
OLIVER, R., 396
OLLSWANG, A. H., 646
OLNICK, H. M., 32
OLSEN, A. M., 38
OLSHAKER, B., 237
OLSON, B. J., 19
OLSON, E. C., 381
OLSSON, O., 29
OLWIN, J. H., 252*
O'NEILL, D., 198, 654*
ONG, S. G., 34
D'ONOFRIO, V., 239
OPDYKE, D. F., 119
OPIE, E. L., 142
OPPENHEIM, E., 39
OPPENHEIMER, M. J., 137, 232
OPSAHL, J. C., 36*
ORIAS, O., 574
ORKIN, L. A., 647
ORSINI, M., 370
ORTEGA, L. G., 577
ORTH, O. S., 15, 576
ORTMANN, A., 253*
OSBORNE, R. L., 203
OSBORNE, S. L., 201*
OSHRY, E., 588
OSMOND, J. D., 396
OSMOND, L. H., 614
OSSIPOVSKI, B., 387
OSTENFELD, I., 527
OSWALD, P. E., 602
OTTE, H., 550
OTTO, G. F., 333*
OTTOMAN, R., 13
OUCHTERLONY, O., 226, 407*
OUNSTED, C., 484
OVERMAN, R. S., 601
OVERMAN, W., 234*
OWENS, W. I., 246
OWREN, P. A., 170, 252

PACKER, H., 203, 440
PACZOWSKY, J., 326
PAGE, I. H., 195, 359
PAGE, J. E., 496*
PAGEL, W., 374
PAHUD, J. J., 616
PAINE, R., 499
PAKESCH, E. F., 317
PALACIOS COSTA, N., 24
PALAZZI, A. S., 620*
PALAZZO, W. L., 592
PALEY, K. R., 127
PALEY, P. Y., 430, 431
PALEY, R. G., 612
PALLARDO PEINADO, L. F., 261
PALMBORG, G., 407*
PALMER, E. D., 303, 637
PALMER, R. S., 622
PALMER, W. L., 71, 284, 287, 289, 636
P'AN, S. Y., 579
PANDALAI, K. M., 128
PANGANIBAN, E. C., 260
PANNIER, R., 668
PANSE, F., 94
PANSY, F., 43
PANTLITSCHKO, M., 635
PANZER, R., 391
PAOLETTI, M., 137*
PAPE, R., 243
PAPPENHEIMER, A. M., 477
PAPPER, E. M., 126*
PARADE, G. W., 219*
PARAF, A., 206
PARAF, J., 649
PARDEE, H. E. B., 374*
PARE, J. A. P., 614
PARISI, P., 80
PARK, W. W., 3
PARKER, L. F. J., 496*
PARKER, M. T., 339
PARKER, R. L., 158
PARKER, R. R., 656
PARRA, Y., 441
PARROT, G., 320*
PARROT, L., 320*
PARSONAGE, M. J., 411
PASCHER, F., 79
PASEYRO, P., 403
PASK, V. M., 607*
PASQUINUCCI, G., 432, 433
PATEL, J. C., 544
PATERSON, J. C. S., 331*
PATNODE, R. A., 330*
PATT, H. M., 239, 590*
PATTERSON, M. C., 616

PATTERSON, P. R., 631
PAUL, L. W., 358
PAUL, W. D., 71, 210
PAULI, R. H., 333, 446*
PAULING, L., 496
PAVEL, I., 118*
PAYNE, E. H., 109, 661, 662
PEABODY, G. E., 191, 472
PEACOCK, W. C., 274, 588
PEALE, A. R., 528
PEARSALL, H. R., 361*
PEARSE, A. G. E., 291
PEARSON, S., 76
PEART, A. F. W., 450, 451
PECORA, L. J., 464
PEDROCHE, A., 260
PEERS, J. H., 538
PEET, M. M., 268
PEIRCE, C. B., 470
PELÁEZ, D., 441
PELIZZARI, G., 206*
PELLEGRINO, V., 438
PELLER, S., 224*
PELLISSIER, A., 319*
PELNAR, P., 452
PELOSIO, C., 373
PEMBERTON, H. S., 271
PEMBERTON, J., 227
PENDERGRASS, E. P., 471
PENFIELD, W., 524
PENNES, H. H., 456
PENROSE, L. S., 5*
PERCIVAL, G. H., 299
PERELMAN, H., 618*
PERERA, G. A., 135
PERETZ, E., 649
PEREZ, E., 486
PÉREZ GALLARDO, F., 321
PERITI, P., 432, 433
PERLMAN, H. H., 189
PERLMANN, G. E., 41
PERLMUTTER, M., 74
PERLOFF, W. H., 184
PERRIN, A., 110
PERRY, J. W., 96
PERRY, S. M., 652
PERRY, W. F., 40*
PERTUISET, B., 590
PETCH, C. P., 409*
PETERS, G. A., 268, 572
PETERS, J. H., 53
PETERS, J. P., 582
PETERSEN, A. B., 68
PETERSEN, I., 9
PETERSON, J. C., 626
PETERSON, M. C., 519
PETERSON, W. G., 347
PETIT-DUTAILLIS, D., 528, 590
PETRIE, P. W. R., 114
PEYTON, W. T., 534
PFÄNDLER, U., 118*
PFEIFER, A., 23
PFUETZE, K. H., 126, 664, 668
PHELPS, E. T., 451*
PHILIP, C. B., 320
PHILIPP, E., 32
PHILIPPOT, E., 11, 156
PHILLIPS, A. P., 458
PHILLIPS, E., 377*
PHILLIPS, S. K., 71*
PIAGGIO BLANCO, R. A., 403
PICKERING, G. W., 286
PIERAERTS, G., 487
PIETROWSKI, J. J., 103
PILCHER, C., 202
PILGERSTORFER, W., 517*
PILON, —, 663
PINAKAPANI, S., 21*
PINES, K. L., 135, 233*
PIPKIN, A. C., 332
PIQUE, J. A., 649
PIRINGER, W., 517*
PIRKEY, E. L., 141
PIRONE, P. P., 319*
PITTMAN, M., 19
PITTS, R. F., 120, 598*
PIZZOLATO, P., 382
PLACE, E. H., 322
PLANSON, E., 544
PLAS, F., 168
PLATAKIS, J., 363
PLATT, W. D., 176, 665
PLATT, W. R., 135
PLESSINGER, V. A., 556*
PLOTZ, C. M., 643
PLOTKE, F., 301, 401, 515
PLUMMER, N., 603
PLUVINAGE, R., 342*
POCHIN, E., 568
POGNAN, C., 118
POKORNÁ, L., 592
POLÁČEK, L., 200
POLLEY, H. F., 110
POLLOCK, L. J., 318
POLONI, A., 206*
POLÓNIO, P., 535
PONDER, R., 118*
DE PONTI, C., 357
POOLE, C. S., 291
POOLE, S. O., 418
POOS, F., 33
POPE, H., 330*
POPOVIĆ-SAVIĆ, J., 435
POPP, W. C., 242
POPPEL, M. H., 356, 634
POPPER, H., 179, 180
PORJÉ, I. G., 493
POROT, M., 655
PORTER, A., 80
PORTER K. R., 568
PORTERFIELD, J. S., 605*
PORTMANN, A. F., 459
PORTMANN, U. V., 396
POSTEL, S., 239
POTTS, W. J., 58
POU DÍAZ, J., 255
POWELL, B. W., 46
POWELL, C. C., 464*
POWER, M. H., 71, 72, 283, 291
POWERS, S. R., 157
DE PRADA, J., 541, 656
PRAIN, J. H., 584*
PRAKKEN, J. R., 510
PRATT, E. L., 197
PRATT, R., 42
PRATT-THOMAS, H. R., 165
PREIFER, C. A., 36*
PRIBILLA, W., 550
PRICE, C. W., 236*
PRICE, H. J., 546
PRICE, I. N. O., 361*
PRICE, P. B., 465
PRICHARD, R. W., 651
PRIETO, G., 29
PRIGAL, S. J., 350
PRIGOT, A., 513
PRINDLE, R. A., 229
PRINZ, F., 582
PRINZMETAL, M., 183*, 378, 379
PRITCHARD, J. A., 66
PRIVITERI, C. A., 634
PRUNTY, F. T. G., 50
PRYOR, H. B., 109
PUCK, T. T., 561
PUGH, L. G. C., 617
PULASKI, E. J., 17, 351
PULLICINO, G. C., 112*
PULLINGER, B. D., 598
PULLMAN, T. N., 284
PULVERMACHER, E., 29
PUMP, K., 614
PUNDEL, P., 623
PUNTIGAM, F., 225, 563
PUTNAM, D. E., 646
PUTNIK, D., 435
PUTSCHAR, W. G. J., 618*

QUADBECK, G., 127
QUASTLER, H., 138
QUICK, A. J., 168, 343*, 361, 568*, 601
QUIEROGA, L. T., 230*
QUILLIAM, J. P., 121
QUIMBY, E. H., 508
QUINLIN, P. M., 249*
QUIVY, D., 570

RAASCHOU, F., 161, 195
RABEN, M. S., 293
RABINER, A. M., 231
RABINOWITCH, I. M., 371
RABY, K., 463
RABY, W. T., 323, 324
RACADOT, —, 208
RACE, G. G., 474*
RACHET, J., 179
RACHMILEWITZ, M., 273
RADENBACH, K. L., 549
RADTKE, F., 526
RADWIN, L. S., 508*
RAFALOVITCH, S. M., 605*
RAFFEL, S., 387
RAGAN, C., 521, 643
RAGNI, M., 349
RAKHMEL, E. A., 148
RALL, J. E., 403
RALLI, E. P., 394
RALPH, P. H., 601*
RALSTON, R. J., 662
RAMACHANDRAN, R., 552
RAMAMURTHI, B., 21*
RAMAN, T. K., 21*
RAMES, E. D., 360
RAMMILKAMP, C. H., 562, 603
RAMOS, J., 621
RAND, C. W., 199
RANDALL, H. T., 596
RANDALL, K. J., 45*, 563
RANDALL, L. O., 347
RANDALL, R., 364*
RANSFORD, P. M., 256
RANSMEIER, J. C., 546
RANSOME, G. A., 331*
RANSTRÖM, S., 488
RANTZ, L. A., 425
RAOUL-DUVAL, —, 167
RAPOPORT, M., 404*
RAPPAPORT, E. M., 39
RAPPAPORT, M. B., 162, 490
RASCOFF, H., 539*
RASHKIND, W. T., 343*
RASKINA-BRAUDE, M. V., 616*
RASMUSSEN, T., 141
RASPONI, L., 295
RATNOFF, O. D., 504
RAUSCHKOLB, J. E., 515
RAUSHENBAKH, M. O., 475
RAVDIN, I. S., 349
RAVINA, A., 84
RAVITS, H. G., 296
RAWLINGS, J. M., 148
RAWLS, N. B., 591
RAWSON, R. W., 588
RAY, C. T., 234*
RAY, L. J., 455
RAYNAUD, J., 396
RAZEMON, P., 668
RAZIMOV, N. P., 390
REA, E. L., 637*
READ, J. T., 62
READER, G., 472
REARDON, M. J., 268
REBELL, G., 297*
V. RECHENBERG, H. K., 426
RECINOS, A., 237
REDFEARN, J. W. T., 351
REDNER, B., 47
REEVES, R. J., 163
REGNA, P. P., 22*, 579
REICHEL, W. S., 470, 637
REICHER, J., 49
REID, D. E., 343*
REID, E., 249*
REID, F., 593
REID, H. A., 54
REIMANN, H. A., 485
REIN, C. R., 516
REINHOLD, J. G., 262
REINHOLD, M., 651
VON REIS, G., 525
REISEL, J. H., 625
REISNER, E. H., 165
REISS, F., 76
REISS, M., 396
REKERS, P., 242*
RELMAN, A. S., 619
RENARD, M., 535
RENNIE, J. B., 491, 634
RENTON, P. H., 343*
REUBI, F. C., 160
REUMONT, M., 204
REXTED, B., 528
REYN, A., 194
REYNES, V., 100
RHANEY, K., 482
RHEINLANDER, H. F., 502
RHOADS, J. E., 391
RHOADS, P. S., 17
RHODHAIN, J., 669
RIBAUDO, C. A., 274
RICCI, N. I., 239
RICE, E. C., 423, 462*, 662
RICE, J. S., 297
RICHARDS, D. W., 173, 458
RICHARDS, H. G., 165
RICHARDS, R. C., 465
RICHARDS, R. K., 122, 368
RICHARDSON, H. L., 68
RICHARDSON, J. S., 532
RICKARD, E. R., 97
RICKER, W., 278
RICKETTS, W. E., 289, 639
RIDDELL ROYSTON, G., 6
RIDER, J. A., 419, 539
RIDER, R. V., 192
RIDOUT, J. H., 595
DI RIENZO, S., 590
RIESEN, D. E., 138
RIGDON, R. H., 331*
RIGGS, D. S., 74
RIGOTTI, S., 202
RIJKEBÜSCH, L., 209
RIKER, W. F., 460
RIKIND, A. V., 281
RILLIET, B., 541
RING, G. C., 137
RINGENBACH, G., 569
RIPLEY, H. S., 533, 654
RIPY, H. W., 626
RISCO, A., 23
RISMAN, G., 486
DE RITIS, F., 541
RITOVA, V. V., 478
RITVO, M., 282
RITZ, N. D., 275
ROBBINS, E., 175
ROBBINS, L. L., 137, 140, 174
ROBERTS, J. I., 441
ROBERTS, K., 290
ROBERTSON, A. M., 512*
ROBERTSON, C. K., 279
ROBERTSON, E. G., 201
ROBERTSON, J. P. S., 535*
ROBERTSON, O. H., 561
ROBIN, E. D., 646
ROBINS, H. M., 86
ROBINSON, C. E., 620
ROBINSON, C. S., 138
ROBINSON, F., 588*
ROBINSON, H. M., 189, 514
ROBINSON, H. M., Jnr., 189, 514
ROBINSON, J. A., 85
ROBINSON, L. B., 405
ROBINSON R. C. V., 189, 191, 303, 514, 646
ROBINSON, R. H. M., 254
ROBSON, H. N., 498
ROBSON, J. S., 250*, 394, 476*
ROBSON, J. T., 462
ROBY, C. C., 343*
ROCHE, —, 431
ROCHE, L., 117
ROCKWOOD, E. M., 296*, 509
RODES, P. J., 471
RODRIGUEZ, J. N., 439
RODRÍGUEZ ARIAS, A., 620*
RODRIQUEZ, J., 401, 515
RODWELL, A. W., 41
ROEMER, G. B., 514
ROEMMELT, J. C., 120, 598*
ROGERS, E., 228
ROGERS, J. V., 31
ROGERS, K. B., 481
ROGERS, W. F., 293, 487, 507
ROGERSON, A. G., 641
ROGOFF, B., 86
ROHR, J. H., 17
ROM, J., 485
ROMANSKY, M. J., 646
ROMBOLD, C., 29*
ROMEO, F., 552
ROSNE, L., 649
ROOFE, P. G., 137
ROOST-PAULI, H., 348
ROOST-PAULI, M., 348
ROOT, H. F., 153
ROOT, M. A., 11
ROOTH, G., 17*
ROSAHN, P. D., 514*
ROSCOE, J. D., 481
ROSE, A. S., 192
ROSE, B., 614, 642

Rose, G. A., 171
Rose, L. M., 127
Rosen, G., 112*, 224*
Rosen, H., 262
Rosenau, B. J., 193*
Rosenberg, E. F., 52
Rosenberg, L. S., 357
Rosenblatt, P., 96
Rosenbloom, S. E., 389
Rosenburg, M. J., 374*
Rosenheim, M. L., 271, 272
Rosenman, R. H., 264
Rosenthal, R. L., 360
Rosenthal, S. R., 274, 278*
Roshchin, V. P., 475
Rosier, M., 411*
Rosin, A., 273
Ross, S., 237, 423, 462, 662
Ross, V., 99, 477
Rossman, I., 588
Rotès, J., 86
Roth, H. H., 468
Roth, L. W., 368
Roth, O., 627
Roth, P., 290*
Rothstein, A., 133
Rottenberg, L. A., 388
Rotter, R., 475
Rottino, A., 65, 274
Rountree, P. M., 362
Rouquès, L., 203
Roussillon, J., 84
Routien, J. B., 579
Routier, D., 378
Rovello, F., 306
Rovelstad, R. A., 180
Rovenstine, E. A., 126*
Roviralta, E., 482
Rowe, C. L., 514*
Rowe, R. J., 193*, 254*
Rowley, D., 581*
Roy, E. C., 260
Rozansky, R., 20, 362*
Rozental, A. S., 148
Rubbo, S. D., 334
Rubenstein, L., 252*
Rubin, E. H., 430
Rubin, L., 190
Rubin, M., 434
Rubin, M. I., 404*
Rubins, J. L., 91
Rubinstein, M. A., 385
Rubio, C., 54
Rubitsky, H. J., 486
Ruby, B., 380
Rudbäck, L., 427
Rudhe, U., 455
Rudney, H., 230*
Ruhe, D. S., 442, 443
Ruiter, M., 511
Ruiz Sánchez, A., 320
Ruiz Sánchez, F., 320
Rule, A. M., 188
Rumball, J. M., 239
Rumyantsev, A. V., 476
Rundles, R. W., 170
Rupp, F., 616
Rusch, H. P., 596
Ruskin, A., 331*, 577*
Russell, B., 49
Russell, D. S., 311
Russell, S. J. M., 666
Russell, W. T., 450
Rust, E., 145
Rustung, E., 345*
Rutberg, F. L., 210
Rutenberg, A. M., 647
Rutledge, D. L., 265
Rutzky, J., 275
Ruys, A. C., 5*
Ryan, M. L., 545
Ryle, J. A., 450

Sabin, A. B., 441*
Sachs, E., 9*
Sadusk, J. F., 104
Saénz, A., 552
Safwat, A., 661
Sahlgren, E., 525
Saint, W. K., 272
Saint-Etienne, J., 100
St. Vincent, L., 579*
Salcedo, J., 260
Salcedo Vega, V., 418*
Sales, L. M., 500*
Salinger, S., 291*
Salisbury, P. F., 624
Salvi, A. E. K., 438*
Salvin, S. B., 144*
Samitz, M. H., 78*
Sampson, J. J., 158
Sams, W. M., 295
Samter, M., 151
Samwick, A. A., 169
Sánchez-Barriga Carapeto, M., 78, 646*
Sancho Martínez, F., 46
Sand, R., 560*
Sandage, C., 145*
Sandblom, P. H., 633
Sanders, M., 239
Sanderson, M., 587*
Sanes, S., 638
Sanjeevarao, P., 552
Sante, L. R., 632
Santos, P. M., 466*
Sapeika, N., 270
Sapero, J. J., 193
Sappington, T. S., 285, 288
Sartorius, O. W., 120, 290, 598*
Sati, M. H., 105
Sattenspiel, E., 476*
Saunders, R. H., 45*
Sautter, V., 603
Savage, M. C., 579*
Savarino, S., 105*
Savilahti, M., 155, 374
Savitt, L. E., 80
Sawchuk, S., 528
Sawitsky, A., 275
Sawtelle, W. W., 571
Sawyer, G. M., 532*
Sawyer, P. N., 391
Scalfi, L., 541
Scarzella, M., 131
Schaefer, H., 54*
Schaefer, R., 399
Schaeffer, M., 419
Schaerer, P., 229
Schaffenburg, C., 183
Schajowicz, F., 649
Schaub, I. G., 238
Scheff, G. J., 601*
Schennetten, F. P. N., 377
Scherf, D., 158, 376, 491*
Scherrer, J., 576
Scheuerman, W. G., 653
Schiele, B. C., 534
Schifani, L., 465*
Schildback, H. R., 141
Schiller, I. W., 485
Schiller, M., 318
Schilling, J. A., 36*
Schilling, R. F., 627
Schipper, G. J., 516*
Schlesinger, B., 85, 264
Schlesinger, M. J., 247*
Schlesinger, R. W., 44, 45
Schlichter, J. G., 129
Schloss, E. M., 368
Schloss, W. A., 647
Schmermund, H. J., 28
Schmid, J. F., 368
Schmidt, C., 508
Schmidt, H., 417
Schmidt, L. H., 128
Schmidt-Voigt, J., 550
Schmitt, F. O., 603
Schmitz, A., 550
Schnabel, T. G., 209
Schneider, W., 510
Schnitzer, R. J., 18
Schober, W., 412
Schoch, A. G., 301, 515
Schoenbach, E. B., 238, 461, 462, 577
Schönfeld, W., 514
Scholtze, H., 436
Schomer, A., 172
Scor, H. C., 7
Schrauzstätter, E., 462*
Schreiber, F. G., 221
Schrenk, H. H., 226*
Schroeder, H. A., 184, 305
Schröder, W., 246
Schubert, M., 221
Schüffner, W., 446
Schulman, J., 635
Schulte, G., 30
Schultz, A. E., 130
Schultz, J., 394
Schulze, W., 152
Schulze-Buschoff, H., 658
Schunk, A., 403
Schwab, H., 415
Schwab, R. S., 414*
Schwarting, V. M., 363
Schwartz, B. M., 277
Schwartz, E., 49, 615
Schwartz, L. L., 378
Schwartz, M., 123
Schwartz, S., 152
Schwartz, S. P., 57
Schwartzman, J., 426
Schwarz, E., 164
Schweinburg, F. B., 647
Schwemlein, G. X., 302, 515
Sciarra, D., 651
Scobey, R. R., 658
Scott, G. D., 363*
Scott, G. E. M., 610
Scott, J. M., 63
Scott, V., 192
Scott, W. G., 594*
Scott, W. W., 77*, 367*, 517
Scott Park, S. D., 634
Scriba, K., 153
Scudamore, H. H., 568
Scudder, H. I., 115
Scudi, J. V., 215
Seabury, J. H., 260
Seaton, D. R., 443
Sebrell, W. H., 1
Seckel, H. P. G., 367*
Sédallian, P., 110
See, J., 445*
Seed, J. C., 578
Seegers, W. H., 456
Seeley, D. B., 579
Segal, M. S., 279, 486, 499
Segers, M., 54, 154
Seidelin, G., 602
Seidlin, S. M., 588
Seifert, M. H., 420
Seifter, J., 649
Seip, M., 429*
Selbie, F. R., 254
Seligmann, E., 131, 647
Selkurt, E. E., 36
Sellei, C., 305
Sellers, E. A., 640
Selwyn, J. G., 64, 343*
Selye, H., 183, 294, 486*, 523
Selzer, A., 492
Seneca, H., 213
Seneviratne, R. D., 230*
Sen Gupta, P. C., 332
Seppelin, D. K., 12
Šercl, M., 651
Servelle, M., 61, 618
Sevin, A., 554
Sevitt, S., 562
Seyss, R., 243
de Sèze, S., 245, 307
Shafer, C. L., 242
Shaffer, C. H., 236*
Shaffer, L. W., 302
Shah, M. J., 322
Shamaskin, A., 665*
Shamesova, L. G., 546
Shanberge, J. N., 168
Shank, R. E., 1
Shapiro, D. M., 577
Shapiro, M. J., 162
Shapiro, S. I., 622
Sharlai, R. I., 636
Sharlit, H., 190
Sharp, A. E., 579*
Sharp, E. A., 109, 164
Sharp, V. E., 579*
Sharpless, N. E., 464*
Shaw, E. W., 322, 539
Shaw, F. H., 570
Shaw, W. M., 126*
Shearman, A. M., 613
Sheehan, D., 386
Sheehan, H. L., 44*, 643
Sheiman, L., 251
Sheinmel, A., 634
Sheldon, W., 47, 610
Shelley, H. M., 563
Shen, J. T. Y., 322
Shenkin, H. A., 653
Shepard, K. S., 236
Shepperd, I. M., 368
Sherman, I. C., 318
Sherman W. B., 151, 613, 644
Shetlar, C. L., 249
Shetlar, M. R., 249
Shevlyagina, M. I., 505
Shields, H. L., 15
Shindledecker, J. B., 193
Shock, N. W., 343, 617
Shookhoff, H. B., 333
Shooter, R. A., 351
Shorr, H. E., 394
Short, D. S., 85*, 319
Short, R. H. D., 259
Shortt, H. E., 558
Shorvon, H. J., 532
Shragg, R. I., 238
Shrewsbury, J. F. D., 447, 559*
Shull, G. M., 579
Shulman, B., 179
Shute, P. G., 449, 558
Shwachman, H., 631
Siebens, A. A., 167
Siegel, E., 588
Siegmund, O. H., 346
Siering, H., 360
Sigmon, H. E., 240, 465*, 584*
Sigwald, J., 413
Šikl, H., 480
Silberberg, M., 597
Silberberg, R., 597
da Silva, M. P., 621
da Silva Lacaz, C., 418*
de Silva, C. C., 556
Silver, C. M., 483
Silverberg, M. G., 79
Silverberg, R. J., 545
Silverman, F. N., 607
Silverman, G., 175
Silverman, J. J., 380
Silverstein, A., 528
Silverstein, M. E., 398
Simkin, B., 183*
Simon, A. J., 267, 378
Simon, M. A., 285
Simon, N., 177
Simon, R. D., 254
Simon, S., 387
Simons, R. D. G. P., 297
Simonton, K. M., 569
Simpson, I. A., 659
Simpson, M. E., 120*
Simpson, R. S., 356
Simpson, S. L., 76
Simrock, W., 542
Simuangco, S., 657
Sinclair, R. J. G., 85*
Singer, C., 336
Singer, I. M., 158
Singer, K., 475
Singer, S. J., 496
Singh, K., 105*
Sirota, J. H., 584*
Sita Lumsden, E. G., 280
Sjaardema, H., 199
Sjögren, B., 76, 119, 160
Sjölin, S., 327
Sjöstrand, T., 455, 457
Skadhauge, K., 349
Skaggs, L. S., 138, 590*
Skinner, C. E., 363
Skipper, H. E., 66
Skouby, A. P., 268
Slack, H. G. B., 62
Slatkin, M. H., 188
Sleator, W., 567*
Sloan, R. D., 517
Slocumb, C. H., 110
Slopek, S., 16
Sluczewski, A., 290*
Smadel, J. E., 320, 323, 402, 420, 421, 660
Smart, G. A., 177
Smellie, J. M., 258*
Smillie, R. A., 450
Smith, A. N., 391
Smith, D. E., 590*
Smith, D. T., 418*

SMITH, E., 96
SMITH, E. L., 496*
SMITH, E. R., 202
SMITH, F. W., 36*
SMITH, H. F., 601
SMITH, H. L., 110
SMITH, H. W., 603
SMITH, I. H., 487*
SMITH, J. C., 227, 340
SMITH, J. F., 50, 211
SMITH, J. R., 499
SMITH, M. I., 328
SMITH, P. H., 603, 604
SMITH, S., 518
SMITHBURN, K. C., 96, 211
SMYTH, N. P. D., 67*
SNAPP, R. H., 512
SNELL, A. C., 36*
SNELL, A. M., 168
SNELL, F. M., 382*
SNIFFEN, R. C., 174, 500
SNODDY, W. T., 58
SNODGRASS, H. M., 639
SNORRASON, E., 522
SNYDER, J. C., 98
SNYDERMAN, S. E., 454
SOBERON, G., 441
SOBIN, B. A., 579
SOETERS, J. M., 47
SOFFER, L. J., 505
SOLDI, A., 465*
SOLOMON, C., 239
SOLOMON, D. H., 305*
SOLOMON, H. C., 192, 410
SOLOMON, W. M., 371
SOLOMONS, I. A., 22*, 579
SOLOVYEV, V. D., 478
SOLWAY, A. J. L., 267
SOLYMOSS, A., 84
SOMMER, E., 592
SOMMER, F., 202
SOMMER, L. S., 235*
SOMMER PEDERSEN, B., 623
SOMMERS, S. C., 474
SONCK, C. E., 334*, 402
SONNENSCHEIN, R. R., 198, 570
SOO-HOO, G., 18
SORKIN, S. Z., 505*
SORREL, A., 349, 542
SORREL, G., 191
SORSBY, A., 17*
SOSMAN, M. C., 185
SOULAIRAC, A., 535
SOULIE, P., 378, 618
SOULIER, J. P., 382
SOUŠEK, O., 636
SOUTHCOTT, R. V., 339
SPALDING, J. M. K., 469
SPAULDING, E. H., 254*
SPEAKMAN, T. J., 567*
SPECTOR, S., 483
SPENCE, M. P., 78
SPENCER, F. C., 157
SPENCER, M. P., 36
SPENDLOVE, G. A., 330*
SPERANSKII, G. N., 148
SPICKNALL, C. G., 444
SPIEGEL, E. A., 88
SPIES, T. D., 166, 276, 306, 411*, 486, 505, 522, 642
SPILLANE, J. D., 205, 307
SPINDLER, M., 586
SPINK, W. W., 323, 438, 450*, 662
SPITZ, E. B., 653
SPITZER, N., 194
SPITZNAGEL, J. K., 364
SPRAGUE, H. B., 162, 490
SPRAGUE, R. G., 294
SPRECHLER, M., 522
SPRENT, J. F. A., 222
SPRITZLER, R., 378, 379
SPRUNT, D. H., 220, 324
SQUIRE, J. R., 239*
STADIE, W. C., 261, 373
STAHLER, N., 108
STANFORD, R. L., 614
STANGL, A., 139
STANIER, J. E., 255
STANKIEWICZ, R., 104
STANLEY, M. M., 506
STANLEY, W. M., 596
STANOJEVIC, L., 616
STANTON, J. B., 469
STANTON, J. R., 60, 125, 161, 493, 573
STARE, F. J., 568
STARK, O. K., 145*
STARK, T. H., 43
STARK, W., 317
STATE, D., 287*, 359
STATS, D., 277, 347
STAUFFER, H. M., 633*
STEADMAN, L. T., 452
STEARNS, E., 410
STECHER, R. M., 371, 405
STEEL, M., 566*
STEENKEN, W., 103
STEEPLES, G. L., 8
STEFANINI, M., 168, 202, 361, 393, 504
STEIGMANN, F., 179, 180
STEIN, G., 355
STEIN, H. J., 182
STEIN, I., 55
STEIN, I. F., 126*
STEIH, T., 387
STEINBACH, M. M., 330*, 430
STEINBERG, B. L., 271
STEINBERG, D. L., 612
STEINBERG, H. S., 644
STEINBERG, I., 266, 357, 472
STEINBROCKER, O., 85, 194
STEINER, A., 163
STEINER, R. E., 55
STEMMERMANN, G. N., 599
STEPTO, R. C., 466*
STERLING, J. A., 197*
STERLING, K., 289, 639
STERNBERGER, L. A., 476
STETTEN, D., 488
STEVENS, C. D., 249*
STEVENS, K., 97
STEVENS, S., 662
STEVENSON, I. P., 316, 533
STEWART, C. P., 250*, 476*
STEWART, D., 112*
STEWART, I. S., 100
STEWART, P. H., 249*
STEWART, S. M., 20, 127
STICKNEY, J. M., 382
STOCK, C. C., 248
STOCK, R. J., 197
STOCKS, P., 564
STODDARD, F. J., 585
STOKES, H. L., 334
STOKES, J., 210, 641
STOKES, J. H., 516
STOLLER, A., 411*
STONES, D. G. H., 20
STONE, H., 183
STONE, H. H., 261*
STONE, R. E., 166, 276, 306, 411*, 505, 522, 642
STONE, S., 538
STOREY, N. E., 437*
STRADE, H. A., 143*
STRANSKY, E., 496*
STRATTON, F., 343*
STRAUB, L. R., 654
STRAUB, M., 325, 428
STRAUBE, G., 554
STRAUBE, R. L., 590*
STRAUS, F. H., 304
STRAUSS, E., 562 603
STRAX, S., 288
STREBEL, J., 336*, 560*
STREITFIELD, F. A., 180
STREITMANN, B., 515
STRICKLAND, B. A., 48
STRIEBICH, M. J., 37*
STRITZLER, C., 78
STROM, L., 427
STRONG, F. G., 121
STRUTZMAN, J. W., 271
STUBBS, L. E., 538*
STUCKI, H., 50
STÜBINGER, H. G., 56
STUECK, G. H., 394
STÜHMER, A., 189
STÜRMER, E., 377
STURM, A., 326
STUTZ, E., 548
SUÁREZ, J. R. E., 174, 385, 457
SUAREZ, R. M., 58*, 486
SUAREZ, R. M., Jnr., 58*
SUBIRIA, R., 54
SUDE, G., 501
SUGAR, M., 407
SUGIURA, K., 248
SULLIVAN, M., 298*
SULLIVAN, T. D., 331
SULZBERGER, M. B., 298, 390
SULZER, R., 40
SUMMERS, V. K., 643
SUNDELIN, F., 85
SUNDERLAND, S., 455
SUSSMAN, M. L., 356
SUTHERLAND, D., 152
SUTTON, H., 672*
SVEC, F. A., 17
SWAIN, H. L., 7, 8
SWAN, H. J. C., 460
SWAN, L. L., 175
SWAN, R. C., 23*
SWANSON, E. E., 125
SWART, E. A., 19
SWARTZ, J. H., 296*
SWEANY, H. C., 433, 551, 665*, 667
SWEET, L. K., 99, 239*, 420, 651
SWEET, R. H., 500
SWEITZER, S. E., 512*
SWELLENGREBEL, N. H., 219
SWENDSIED, M. E., 165
SWENSON, O., 502
SWENSSON, A., 134
SWIFT, M. N., 239, 590*
SWIFT, H. F., 223
SWIFT, W. E., 104, 105*
SWINYARD, E. A., 10
SWITZER, P. K., 165
VON SYDOW, G., 488
SYKES, E. M., 162
SYLVÉN, B., 243
SYLVEST, O., 275
SYMINGTON, T., 60, 421
SZÁK, J., 90
SZASZ, T. S., 287, 512*
SZERB, J., 574
SZÉREMI, K., 625
SZONTÁGH, F., 640
SZÜCS, S., 342

TAGER, M., 144*
TAGGART, S. R., 516, 646
TAGNON, R., 293, 507
TAKACS, W. S., 319*
TALBOT, D. R., 529
TALBOT, J. C., 384
TALBOTT, J. H., 489, 581
TALIAFERRO, L. G., 331
TALIAFERRO, W. H., 331
TANRET, P., 84
TANTRET, P., 658*
TAPTAS, J. N., 229, 494*
TAQUINI, A. C., 174, 385, 457
TARA, S., 6
TARACENA DEL PINAL, B., 46
TARAIL, R., 403
TARGOWLA, R., 313
TARTARINI, E., 392*
TAT, R., 167*
TATLOCK, H., 603
TATTERSALL, W., 101
TATTING, B., 383
TAUSSIG, H. B., 58
TAYLOR, A. B., 110*, 294
TAYLOR, G. F., 368
TAYLOR, H., 51
TAYLOR, H. L., 511, 611
TAYLOR, J., 46
TAYLOR, M., 313
TEBBUTT, A. H., 624
TEBROCK, H. E., 658
TEGLBJAERG, H. P. S., 206*
TEGNER, W., 198
TEITELBAUM, M. D., 608
TELFER, S. V., 454
TELLO ORTIZ, A., 210
TENNENT, E. C., 527
TEODORI, M. I., 159
TERRANOVA, R., 491*
TERRY, L. L., 444
TERZIAN, L. A., 108
THAYER, J. M., 611
THAYSEN, E. H., 370
THAYSEN, J. H., 370
THÉROND, C., 551
THIERSCH, I. B., 386
THIMANN, J., 416
THO, A., 502
THOMAS, E. W., 302, 516
THOMAS, N., 404*
THOMPSON, A. W. S., 5
THOMPSON, B., 630
THOMPSON, B. F., 483
THOMPSON, C. R., 121
THOMPSON, E. A., 138
THOMPSON, E. C., 341
THOMPSON, F. A., 513
THOMPSON, W. S., 380
THOMSEN, G., 283
THOMSON, A. P., 1, 113
THOMSON, D. R., 419
THOMSON, E. F., 362
THOMSON, M. L., 275
THORLEY, A. S., 655
THORN, G. W., 518, 633*
THREEFOOT, S. A., 234
THUILLIEZ, A. C., 382*
THUNE, R., 667
THYGESEN, P., 201*, 370
TIBBETTS, R. W., 622
TIFFENEAU, R., 457
TIGAY, E. L., 318
TIKHANOVICH, G. S., 181
TIKHOMIROVA, N. P., 453
TILL, K., 351
TILLEMA, S., 625
TILLISCH, J. H., 242
TILLMANN, W. R., 414*
TIMIRAS, P. S., 183, 294
TIMO IARIA, S., 418*
TIMONEN, S., 486
TISDALL, F. F., 1
TISHLER, M., 22*
TISON, F., 150
TOBIAS, J. M., 239
TOCHOWICZ, L., 161
TOCKER, A. M., 68
TODD, R. MCL., 104
TÖBEL, F., 203
TOLLSTRUP, J., 129
TOLONE, S., 329*
TOLOT, F., 117
TOLUBEEVA, N. A., 270
TOM, J., 99
TOMAN, J. E. P., 10
TONGE, J. I., 26
TOOMEY, J. A., 200*, 319*, 419
TORDA, C., 412
TORGERSEN, J., 118*
TORNAY, A., 528
TÖRNBLOM, N., 8*
TÖRNELL, E., 65, 667
TORSUEV, N. A., 560*
TOSTI, A., 644*
TOTH, F. M., 8
TOTTER, J. R., 64*
TOURAINE, A., 398, 509
TOURNEUR, R., 651*
TOWERY, B. T., 293, 507
TRAEGER, C. H., 85
TRAINER, R. Y., 364
TRAUB, R., 320
TRAUT, E. F., 264
TRAUTMANN, F. O. P., 377
TRAUTWEIN, W., 54*
TRAVIA, L., 373
TRELOAR, A. E., 287*
TREMBLEY, H. L., 671
TREON, J. F., 240, 465*, 584*
TRIBUKH, S. L., 453, 547
TRICE, E. R., 303
TRICOIRE, J., 214, 429
TRIM, A. R., 220
TRIPI, H. B., 87
TROISI, F. M., 232
TROLLE, R., 536
TROLLIET, I., 517
TRONC, J., 219*
TRONSTEIN, A. J., 398
TROSSBACH, J., 576
TROTTER, W. R., 640
TROUNCE, J. R., 67
TRUELOVE, S., 70
TRUMP, J. G., 137
TRUNNELL, J. B., 588
TS'AO, Y. P., 543*
TSEVRENIS, H., 382*
TUBANGUI, M., 446
TUCHMAN, M. S., 623
TUCKER, F. C., 656

TUCKER, H. ST. G., 293
TUCKER, W. B., 666
TUCKER, W. I., 415
TULLIS, J. L., 469
T'UNG, T., 543*
TUOHY, J. H., 4
TURNER, C. N., 179
TURNER, G. C., 433, 551, 667
TURNER, H. M., 451
TURNER, J. W. A., 206
TWIBLE, E., 237
TYLER, F. H., 650
TYREE, E. B., 590*
TZANCK, A., 423

UEHLINGER, E., 624
UMBREIT, W. W., 603, 604
UNDERWOOD, E. A., 112*
UNDERWOOD, G. B., 510
UNGAR, J., 21, 580
UNGER, J. L., 25*
UNGLEY, C. C., 525, 626
UNNA, K., 575
UNTERMAN, D., 233
UPWARD, M. G., 419
URBAN, H., 309
URELES, A., 74
URINSON, Y. P., 269
URWITZ, S., 425
USTVEDT, H. J., 325, 435

VACCARI, R., 644
VAHLQUIST, B., 147, 496
VAISMAN, A., 437, 645, 660
VAKIL, R. J., 321
VALLEE, B. L., 63
VALLEGIANI, L., 669
VALLENTIN, G., 667
VALLERY-RADOT, P., 560*
VALLETTE, F., 14
VANATTA, J., 83, 380
VAN BEEK, C., 600
VAN BOGAERT, L., 309
VAN BOLHUIS, J. H., 47
VANCURA, A., 305
VANDENBROUCKE, J., 628
VAN DER GHINST, M., 342*
VANDERHAEGHE, H., 131
VAN DER SCHEER, J., 97
VANDER VEER, J. B., 617
VAN DOMMELEN, C. K. V., 627
VAN EGMOND, A. A. J., 454*
VANĚK, J., 37
VAN LIERE, E. J., 574
VAN LOGHEM, J. J., 47, 64
VAN ORDSTRAND, H. S., 340
VAN ROOYEN, C. E., 363*
VAN SLYKE, D. D., 602
VAN VLOTEN, T. J., 510
VAN WIEN, H., 104*
VAN ZANDT HAWN, C., 568
VARANGOT, J., 593
VARAY, A., 289*
VARGAS, L., 261
VARSVIK, P., 325
VASILYEVA, K. P., 390
VASS, A., 618*
VAUGHAN, J. H., 363
VEENEKLAAS, G. M. H., 47
VELLA, L., 461
VELU, H., 130
VENTURA, S., 8*, 277
VERA, A. R., 519
VERBEKE, R., 13, 123, 233*, 575
VERDECCHIA, G. C., 592
VERDER, A. E., 662
VERMEERSCH, R., 597
VERNANT, P., 384, 658*
VERNON, S., 117
VESSEY, R. E., 125
VICKERS, H. R., 296*
VIDAL-BARRAQUER, F., 620*
VIDAL-COLOMER, E., 635
VIDEBÆK, A., 521
VIETS, H. R., 224*, 560*
VIETS, W., 436
VIGLIANI, E. C., 116
VIKING, B., 579
VILANOVA, X., 17*, 78, 292
VILARROEI, M. S., 661
VILLALON, F. T., 45*
VILLAMIL, A., 385
VILLAVERDE, M., 75
VILLELA, G. G., 230*
VINCENT, D., 250*
VINSON, J. W., 579
VISLOCKY, K., 135
VITÉZ, I., 625
VITTONE, G., 660
VIVARELLI, I., 79
DE VLEESCHHOUWER, G. R., 575
VÖLKER, R., 379
VOETMANN, E., 229*
VOGEL, E., 536
VOGELSANG, T. M., 44*
VOGL, A., 203, 489*
VOGT, A., 473
VOIGT, G. E., 360
VOLKMANN, M., 376
VONDERHEIDE, E. C., 164
VON GLAHN, W. C., 476
VOORHEES, W. D., 451*
VORDERWINKLER, K., 314
VOTAVA, Z., 123
VOTH, H. W., 324*
VROMAN, G. M. S., 272, 490
VROMAN, L., 272, 490

WADDELL, W. R., 500
WADE, H., 560*
WAGLEY, P. F., 167
WAHLGREN, F., 478
WAIFE, S. O., 153, 505
WAKELEY, J. C. N., 560*
WAKIM, K. G., 268, 572
WAKSMAN, S. A., 19, 237, 329
WALDO, J. F., 129
WALKER, A. E., 524
WALKER, A. J., 163
WALKUP, H. E., 553
WALLACE, D. A., 296
WALLACE, R. B., 219
WALLER, M., 168*
WALLER, R. K., 168*
WALLERSTEIN, R. S., 462*
WALLEY, A., 128
WALLIS, A. D., 648
WALLMARK, G., 565
WALLMARK, I. G., 461
WALSH, J. P., 54, 156
WALTER, K., 526
WALTER, R. I., 291
WALTERS, J. H., 556
WALTERS, W., 71*, 391
WALTHER-BÜEL, H., 315
WALTON, M., 565
WAMMOCK, V. S., 513
WANG, C. F., 289
WANGENSTEEN, O. H., 287*
WANNAMAKER, L. W., 236
WANNAN, J. S., 26
WANTA, R. C., 452
WARD, H. P., 36, 154
WARE, A. G., 456
WARE, P. F., 38
WARIN, R. P., 49
WARMING-LARSEN, A. A., 504*
WARNER, A. R., 364*
WARRACK, G. H., 146
WARREN, J. E., 518
WARREN, M. R., 121
WARREN, S., 468, 474
WARTENBERG, R., 89
WARTER, P. J., 649
WASHBURN, A. M., 4
WASHINGTON, J. A., 423, 462*, 662
WASSÉN, E., 522
WASSERMANN, M., 131, 647
WASSINK, W. F., 632
WATERS, L. L., 582
WATKINS, A. G., 365
WATKINS, A. L., 241
WATKINS, C. H., 66
WATKINSON, G., 222
WATROUS, J. B., 497
WATSON, C. J., 39, 152
WATSON, D. C., 271
WATSON, G. M., 166
WATSON, J. A., 646
WATT, J., 565
WATTS, R. W. E., 209
WAUGH, D., 36*
WAYNE, E. J., 127, 580, 640
WEATHERSBY, A. B., 108
WEAVER, F. L., 341
WEBB, R. R., 208
WEBER, E. J., 608
WEBSTER, B., 191, 472
WEBSTER, D. R., 71*
WEBSTER, J. R., 644
WEDEKIND, T., 549*
WEENS, H. S., 31, 32
WEETCH, R. S., 209
WEGELIUS, C., 469*
WÉGRIA, R., 36, 154
WEICHSEL, M., 236
WEICKHARDT, G. D., 534
WEIDEN, S., 40, 143*, 179
WEIL, M. P., 245
WEILL-HALLÉ, B., 326
WEINER, A. E., 343*
WEINER, D., 611
WEINER, H. M., 158
WEINSTEIN, E. A., 53
WEINSTEIN, S., 401
WEINSTEIN, W. W., 56
WEIS, —., 275
WEISBERG, H. F., 372
WEISER, R. S., 579*
WEISFUSE, L., 387
WEISS, H. A., 39, 170
WEISS, L., 599
WEISSBERG, G., 186
WEISSBERG, J., 613
WEISZ, R., 305
WEITZ, W., 9*
WELCH, H., 236*, 516
WELLER, T. H., 419*
WELLS, A. Q., 3
WELLS, B. G., 162
WELLS, E. B., 174, 461, 631
WELLS, H. S., 263
WELLS, I. C., 496
WELSH, J. H., 13
WELTON, D. G., 298*
WENER, J., 83, 285, 404
WERGELAND, H., 435
WERKÖ, L., 230
WERNER, H. W., 121, 460*
WERNER, S. C., 508
WERNSDÖRFER, R., 512
WERNSTEDT, W., 565
WESCOE, W. C., 460
WEST, E. J., 540
WEST, H. F., 87*
WEST, P. M., 475
WEST, R., 165
WEST, R. M., 513
WESTER, M. R., 232
WESTMAN, A., 291
WESWATER, J. O., 529
WETMORE, P. W., 364*
WETZEL, N. C., 487*
WEXLER, H., 226*
WEYER, F., 98
WEYMES, C., 565
WHARTON, G. K., 620
WHEELER, C. M., 98
WHELTON, R. L., 239*, 420
WHITE, C. M., 29*
WHITE, E., 482
WHITE, P., 372
WHITE, P. D., 619
WHITE, W. F., 627*
WHITEHEAD, J. E. M., 253
WHITEHEAD, W. H., 402*
WHITESELL, F. B., 168
WHITFIELD, A. G. W., 259
WHITNER, V. S., 372
WHITTINGHAM, H., 338*
WHITTINGTON, R. B., 252
WHITTY, C. W. M., 312, 313
WHITWELL, F., 44*
WICHELHAUSEN, R. H., 405
WICKE, G., 343
WIENER, A. S., 25*
WIESINGER, K., 376
WIESMANN, R., 586
WIGGALL, R. H., 303
WIGLESWORTH, F. W., 388
WIGLEY, J. E. M., 399
WIGOD, M., 118*
WILANDER, O., 334
WILDER, R. M., 1
WILDFÜHR, G., 211, 212
WILHELM, S. F., 647
WILKINS, R. W., 54, 59, 161, 493
WILKINSON, J. F., 62, 383
WILKINSON, K. D., 560*
WILKINSON, M., 469
WILL, L., 502
WILLCOX, R. R., 300, 400, 402, 559*
WILLIAMS, E. O., 370
WILLIAMS, G. E. O., 370
WILLIAMS, I. G., 30
WILLIAMS, R. E. O., 561
WILLIAMS, R. H., 164, 293, 507
WILLIAMS, R. J., 152
WILLIAMS, R. W., 136
WILLIAMS, S., 99
WILLIAMS, Y. J., 606
WILNER, D., 358
WILSON, B. J., 361*
WILSON, J. F., 399
WILSON, R. C., 345
WILSON, R. H., 263
WILSON, S. G., 220*
WILSON, S. J., 169
WILSON, T. H., 249
WILSON, T. M., 40*
WILSON, V. K., 275
WILSON, W. M., 437
WILSON, W. W., 129
WILT, J. C., 450
WILTNER, W., 250
WIMER, B., 167*
WINBLAD, S., 334
WINDSOR, T., 13
WINIK, I. W., 458*
WINKELMAN, N. W., 529
WINKLER, W., 536
WINTER, L., 509
WINTROBE, M. M., 383, 650
WIRTS, C. W., 71
WISE, C. S., 241
WISE, H., 561
WISEMAN, B. K., 62
WISSMER, B., 392
WITH, T. K., 522
WITTEKIND, D., 632
WITTS, L. J., 166, 277
WOHL, M. G., 153
WOLARSKY, W., 393
WOLF, B. S., 452
WOLF, F. J., 22*
WOLF, S., 504*, 533, 654
WOLF, W. H., 90
WOLFF, H. G., 89, 316, 412, 532, 533
WOLFF, H. H., 568
WOLFF, W. A., 540
WOLFSOHN, G., 182
WOLFSON, W. Q., 52, 314
WOLINSKY, E., 103
WOLL, F., 252*
WOLLAEGER, E. E., 71, 72, 283
WOLMAN, L., 409
WOLTMAN, H. W., 412
WONG, Y. T., 203
WOOD, D. R., 122
WOOD, E. E., 384
WOOD, E. H., 140, 345
WOOD, E. J., 282, 341
WOOD, I. J., 143*, 179
WOOD, P., 266
WOOD, W. J., 450
WOODHALL, B., 129
WOOD JONES, F., 224*
WOODRUFF, A. W., 332
WOODRUFF, C. E., 104, 626
WOODS, M. W., 229
WOODWARD, T. E., 237, 320, 323, 324, 421, 660
WOOLDRIDGE, W. E., 297
WOOLF, B., 269
WOOLNER, L. B., 282
WRIGHT, H., 584*
WRIGHT, H. P., 577
WRIGHT, I. S., 601
WRIGHT, J., 46
WRIGHT, L. T., 288, 513
WRIGHT, S., 123
WRIGHT, W. S., 290
WU, T. T., 106*
WUHRMANN, F., 382
WULFF, M. H., 370
WUNDERLY, C., 382
WYCIS, H. T., 88

WYLLIE, W. G., 367
WYMAN, L., 605
WYNDHAM, C. L., 617
WYNN, W., 566
WYSS, F. 50

XALABARDER, C., 629

YAGER, R. H., 249*
YAKUSHEVA, T. S., 248
YANNITELLI, S. A., 104
YEOMANS, A., 98
YESNER, R., 394
YOUNG, B. R., 471
YOUNG, C. J., 40
YOUNG, E. H. P., 437*
YOUNG, F. G., 249*
YOUNG, F. H., 103
YOUNG, M. D., 443
YOUNG, M. Y., 127
YOUNG, R. M., 417
YOUNG, W. F., 606
YOUNGWIRTH, S. H., 489*
YOUNKER, W. J., 240
YOUNKERS, W., 465*
YOUNT, E. H., 443
YOW, E. M., 323
YUDA, N. N., 125

ZAFFAGNINI, V., 607
ZAGARIA, R., 152
ZAGER, L. L., 572
ZAHALAN, F., 489
ZAHN, D. W., 500*
ZAJACZKOWSKI, H., 23
ZAK, F. G., 298, 598
ZAMCHECK, N., 289
ZAMECNIK, P. C., 1
ZAMORA, G. M., 661
ZANETTI, E., 357
ZANUSSI, C., 656*
ZARAFONETIS, C. J. D., 98
ZÁRATE, O., 260*
ZARDAY, I., 54*
ZARETSKII, I. I., 466
ZARIBNICKY, F., 449
ZDANSKY, E., 218
ZEDER, E., 243
ZEGLIO, P., 464
ZELLER, W. W., 85
ZELLWEGER, H., 201*
ZETTERBERG, B., 105*
ZHEUTLIN, B., 160*
ZHEUTLIN, H. E. C., 191, 303
ZIEGLER, D. K., 413
ZIEGLER, M. R., 290
ZILLIACUS, H., 486
ZIMDAHL, W., 378
ZIMERINOV, A. A., 605*
ZIMMERMAN, H. M., 430
ZINI, F., 430
ZINKHAM, W. H., 167
ZINNEMANN, K., 254
ZINS, E. I., 403
ZINTEL, H. A., 349
ZOLLINGER, H. U., 247
ZONDEK, H., 182, 261
ZUBROD, G., 22*
ZUCKERMAN, R., 260*, 369
ZÜLCH, K. Z., 310
ZUELZER, W. W., 353, 390
ZVETINA, J. R., 665*
ZWEIFACH, B. W., 10

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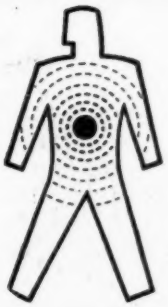
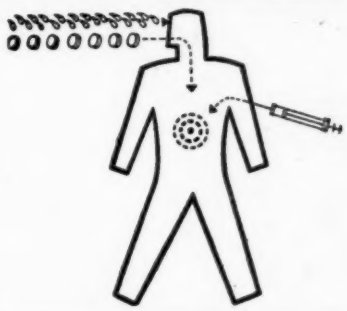
Histamine is released in allergy and produces its effects (A) LOCAL
(Intrinsic histamine)

(B) REMOTE
(Extrinsic histamine)



Antihistamines abolish the effects of extrinsic histamine by blocking the tissue receptors



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